Historic, archived document

Do not assume content reflects current scientific knowledge, policies, or practices.

aSF601
.A1U5

APHIS 91-31

U.S. DEPT. OF AGRICULTURE
NAT'L AGRIC. LIBRARY

APR 11 '77

PROCUREMENT SECTION
CURRENT SERIAL RECORDS

FIELD
OPERATIONS
MANUAL

BIOLOGICS PROGRAM

February 1977
Veterinary Services
Animal and Plant Health
Inspection Service

United States
Department of
Agriculture

FIELD OPERATIONS MANUAL

BIOLOGICS PROGRAM

VETERINARY SERVICES

ANIMAL AND PLANT HEALTH INSPECTION SERVICE

UNIT INDEX

1. Introduction
2. Authority for Biologics Program Field Activities
3. Specific Interpretation of the Regulations
4. Inspection of Establishments
5. Investigation and Processing of Alleged Violations of the Virus-Serum-Toxin Act
6. Handling of Consumer Complaints Involving Biologics
7. Product Release/Other Area Office Procedures
8. Product Sampling
9. Product Destruction

INTRODUCTION

OBJECTIVES

1. The Mission of the Inspector in Historical Perspective - the need to regulate the production and sale of veterinary biologics has been recognized in the United States since the turn of the century. As early as 1902, attempts were made to link an outbreak of foot and mouth disease in the New England states to smallpox vaccine imported from Japan. During FY 1909, the Biochemic Division of the Bureau of Animal Industry (BAI) tested hog cholera vaccines and serums, tetanus antitoxins and "a serum for the prevention of infectious abortion in cattle" for effectiveness and safety. These products varied widely in potency. The "serum" for infectious abortions was actually a weak solution of carbolic acid! In 1906, Drs. Dorset, Niles, and McBride of the BAI had obtained a patent on production of anti-hog cholera serum which, when properly produced, offered help to the many farmers whose herds were being stricken with the disease. Unfortunately, many of the serums that were being sold were not being properly produced. By 1913, sufficient proof had been offered to Congress by disease control officials to convince the Congress that legislation to regulate veterinary biologics production was necessary. On March 14, 1913, in the administration of Woodrow Wilson, the appropriations bill passed for the Department of Agriculture for FY 1914 contained what is now known as the Virus-Serum-Toxin Act of 1913 (V-S-T Act).

The first full-time biologics inspector, Dr. F. A. Imler, was detailed to establishment inspection from the National Stockyards at Chicago on October 27, 1913.

Key phrases within the V-S-T Act are " . . . it shall be unlawful . . . to prepare . . . any worthless, contaminated, dangerous or harmful . . . virus, serum, toxin or analogous product intended for use in . . . animals."

The mission of the inspector today remains the same one assigned to Dr. Imler in 1913 . . . to help carry out this mandate assigned to USDA in the Virus-Serum-Toxin Act.

2. Purpose of the Manual - The working details used for conducting the Biologics Program Field activities are obtained from many sources. Some of the most useful basic sources are:

1. The Virus-Serum-Toxin Act itself.
2. Regulations contained in Title 9, Chapter I of the Code of Federal Regulations (recent amendments are especially important) including:
    a. Subchapter E, Parts 101-117, 122, 123 containing the Biologics Program regulations (plus regulations on Organisms and Vectors).
    b. Subchapter A, Parts 1-4 containing regulations governing the Laboratory Animal Welfare Act.
3. Veterinary Services Memoranda in the 800 series.
4. Veterinary Services Biologics Notices.
5. Numerous other specific sources such as licenses, outlines of production, and Veterinary Services Laboratories (VSL) Supplemental Assay Methods (SAM's).

This manual will not serve as a substitute for these basic sources. It is designed to integrate many diverse fragments of information into a single entry that, hopefully, will emerge as a useful working tool for conducting meaningful and productive inspections and other field activities.

The manual has purposely been designed to fit into a three ring notebook binder. To maintain its usefulness, pages will be added, deleted, or modified as changing circumstances dictate.

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 2
AUTHORITY FOR BIOLOGICS PROGRAM FIELD ACTIVITIES

AUTHORITY FOR BIOLOGICS PROGRAM FIELD ACTIVITIES

CONTENTS

Page
CONSTITUTIONAL BASIS.......... 2
VIRUS-SERUM-TOXIN ACT.......... 2
RELATED STATUTES.......... 2
U.S. CODE ANNOTATED.......... 2
RULES AND REGULATIONS.......... 2
  Virus-Serum-Toxin Act Authority.......... 2
  Administrative Procedure Act.......... 2
  Federal Register.......... 2
  Code of Federal Regulations.......... 2
RESPONSIBILITIES AND AUTHORITIES FOR THE BIOLOGICS PROGRAM.......... 3
  Staff and Laboratory Activities (VS Memo 800.1).......... 3
  Line Activities (VS Memo 800.2).......... 3

AUTHORITY FOR BIOLOGICS PROGRAM FIELD ACTIVITIES

CONSTITUTIONAL BASIS

The authority for the Biologics Program is ultimately derived from Article I, Section 8, clause 18 of the United States Constitution, which empowers Congress to enact all laws which may be necessary and proper to carry into effect the powers expressly granted to it.

More specifically, Veterinary Services, Animal and Plant Health Inspection Service, is operating under delegated authority from the Secretary of Agriculture in administering the following statutes enacted by Congress.

VIRUS-SERUM-TOXIN ACT

21 USC 151-158	"The Virus-Serum-Toxin Act."
7 USC 430	Purchasing and Testing of Serums or Analogous Products; Dissemination of Test Results.

Copies are attached as Figures 2-1 and 2-2.

RELATED STATUTES

There are several statutes that regulate activities closely related to activities involving administration of The Virus-Serum-Toxin Act. Among these statutes are:

21 USC 301-392	"The Food, Drug, and Cosmetic Act"
15 USC 1459	"The Fair Packaging and Labeling Act"
42 USC 262	Regulation of Biological Products and Clinical Laboratories and Control of Radiation
18 USC 832	Transportation of Explosives, Radioactive Materials, Etiologic Agents, and other Dangerous Articles

U.S. CODE ANNOTATED

Additional information about various statutes less directly related to the Virus-Serum-Toxin Act can be obtained by consulting the United States Code Annotated (USCA). Sets of USCA can usually be found in large municipal or university libraries. USCA contains a General Index which is a valuable aid in locating statutes governing specific topics of interest.

RULES AND REGULATIONS

Virus-Serum-Toxin Act Authority

Administrative Procedure Act

Federal Register

The Secretary of Agriculture is authorized in the Virus-Serum-Toxin Act (in 21 USC 154) to make and promulgate from time to time such rules and regulations as may be necessary. The Administrative Procedure Act (5 USC 551 et. seq.) specifies the general guidelines for document preparation and publication of rules and regulations. In brief, the Administrative Procedure Act requires general notice of proposed rule making to be published in the FEDERAL REGISTER and requires publication of all important rules not less than 30 days before their effective date. All rules are subsequently published in yearly updates of the CODE OF FEDERAL REGULATIONS (CFR).

Code of Federal Regulations

Rules and regulations governing the administration of the Virus-Serum-Toxin Act are found in Title 9 of CFR in Parts 101-123.

It goes without saying that a thorough, accurate, and timely knowledge of all regulations in 9 CFR 101-123 is mandatory in order to carry out your duties effectively in Biologics Program Field Activities. When activities require a knowledge of other portions of the CFR, a Table of CFR Titles and Chapters, which has been placed at the back of each of the paperbound CFR titles should be consulted. Again, most large municipal and university libraries contain a full set of the CFR.

RESPONSIBILITIES AND AUTHORITIES

Veterinary Services Memoranda	Responsibility and authority for various specific actions under the Virus-Serum-Toxin Act is delegated to the Deputy Administrator within 9 CFR 101-123. Staff, laboratory, and line activities are further defined in two Veterinary Service Memorandums: 800.1 for staff and laboratory and 800.2 for line or field activities.

UNITED STATES CODE
CHAPTER 5 - VIRUSES, SERUMS, TOXINS, ANTITOXINS, AND ANALOGOUS PRODUCTS

Sec.

151. Preparation and sale of worthless or harmful products for domestic animals prohibited; preparation to be in compliance with rules at licensed establishments.
152. Importation regulated and prohibited.
153. Inspection of imports; denial of entry and destruction.
154. Regulations for preparation and sale; licenses.
155. Permits for importation.
156. Licenses conditioned on permitting inspection; suspension of licenses.
157. Same; inspection daytime or nighttime.
158. Offenses; punishment.

(37 Stat. 832-833; 21 U.S.C. 151-158).

§ 151. Preparation and sale of worthless or harmful products for domestic animals prohibited; preparation to be in compliance with rules at licensed establishments.

It shall be unlawful for any person, firm, or corporation to prepare, sell, barter, or exchange in the District of Columbia, or in the Territories, or in any place under the jurisdiction of the United States, or to ship or deliver for shipment from one State or Territory or the District of Columbia to any other State or Territory or the District of Columbia, any worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous product intended for use in the treatment of domestic animals, and no person, firm, or corporation shall prepare, sell, barter, exchange, or ship as aforesaid any virus, serum, toxin, or analogous product manufactured within the United States and intended for use in the treatment of domestic animals, unless and until the said virus, serum, toxin, or analogous product shall have been prepared, under and in compliance with regulations prescribed by the Secretary of Agriculture, at an establishment holding an unsuspended and unrevoked license issued by the Secretary of Agriculture as hereinafter authorized.

§ 152. Importation regulated and prohibited.

The importation into the United States, without a permit from the Secretary of Agriculture, of any virus, serum, toxin, or analogous product for use in the treatment of domestic animals, and the importation of any worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous product for use in the treatment of domestic animals, are hereby prohibited.

§ 153. Inspection of imports; denial of entry and destruction.

The Secretary of Agriculture is hereby authorized to cause the Bureau of Animal Industry to examine and inspect all viruses, serums, toxins, and analogous products, for use in the treatment of domestic animals, which are being imported or offered for importation into the United States, to determine whether such viruses, serums, toxins, and analogous products are worthless, contaminated, dangerous, or harmful, and if it shall appear that any such virus, serum, toxin, or analogous product, for use in the treatment of domestic animals, is worthless, contaminated, dangerous, or harmful, the same shall be denied entry and shall be destroyed or returned at the expense of the owner or importer.

§ 154. Regulations for preparation and sale; licenses.

The Secretary of Agriculture is hereby authorized to make and promulgate from time to time such rules and regulations as may be necessary to prevent the preparation, sale, barter, exchange, or shipment as aforesaid of any worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous product for use in the treatment of domestic animals, and to issue, suspend, and revoke licenses for the maintenance of establishments for the preparation of viruses, serums, toxins, and analogous products, for use in the treatment of domestic animals, intended for sale, barter, exchange, or shipment as aforesaid.

§ 155. Permits for importation.

The Secretary of Agriculture is hereby authorized to issue permits for the importation into the United States of viruses, serums, toxins, and analogous products, for use in the treatment of domestic animals, which are not worthless, contaminated, dangerous, or harmful.

§ 156. Licenses conditioned on permitting inspection; suspension of licenses.

All licenses issued under authority of this chapter to establishments where such viruses, serums, toxins, or analogous products are prepared for sale, barter, exchange, or shipment as aforesaid, shall be issued on condition that the licensee shall permit the inspection of such establishments and of such products and their preparation; and the Secretary of Agriculture may suspend or revoke any permit or license issued under authority of said chapter, after opportunity for hearing has been granted the licensee or importer when the Secretary of Agriculture is satisfied that such license or permit is being used to facilitate or effect the preparation, sale, barter, exchange, or shipment as aforesaid, or the importation into the United States of any worthless, contaminated, dangerous, or harmful virus, serum, toxin, or analogous product for use in the treatment of domestic animals.

§ 157. Same; inspection daytime or nighttime.

Any officer, agent, or employee of the Department of Agriculture duly authorized by the Secretary of Agriculture for the purpose may, at any hour during the daytime or nighttime, enter and inspect any establishment licensed under the provisions of this chapter where any virus, serum, toxin, or analogous product for use in the treatment of domestic animals is prepared for sale, barter, exchange, or shipment as aforesaid.

§ 158. Offenses; punishment.

Any person, firm, or corporation who shall violate any of the provisions of this chapter shall be deemed guilty of a misdemeanor, and shall upon conviction, be punished by a fine of not exceeding $1,000 or by imprisonment not exceeding one year, or by both such fine and imprisonment, in the discretion of the court.

UNITED STATES CODE
TITLE 7 - AGRICULTURE
CHAPTER 17 - MISCELLANEOUS MATTERS

Sec.

430. Purchasing and Testing of serums or analogous products; dissemination of test results

(58 Stat. 734; 7 U.S.C. 430).

The Secretary of Agriculture may purchase in the open market from applicable appropriations samples of all tuberculin, serums, antitoxins, or analogous products, of foreign or domestic manufacture, which are sold in the United States, for the detection, prevention, treatment, or cure of diseases of domestic animals, test the same, and disseminate the results of said tests in such manner as he may deem best.

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 3
SPECIFIC INTERPRETATION OF THE REGULATIONS

Issued:
Supersedes:

SPECIFIC INTERPRETATION OF THE REGULATIONS

CONTENTS

Page

INTRODUCTION - DEFINITIONS.......... 2
LICENSES AND PERMITS.......... 2
  Establishment License.......... 2
  Product License.......... 2
  Product License (Special).......... 3
  Biological Product Permits.......... 3
FACILITY REQUIREMENTS.......... 4
  Plot Plans, Blueprints, and Legends.......... 4
  Building Construction.......... 4
  Personnel and Product Movement.......... 4
  Heating, Ventilation, and Plumbing.......... 4
  Facilities for Virulent or Dangerous Organisms.......... 5
  Dressing Rooms, Toilets, and Lavatory Facilities.......... 5
SANITATION.......... 5
PERSONNEL AT LICENSED ESTABLISHMENTS.......... 5
LABELS.......... 6
PRODUCTION REQUIREMENTS.......... 6
PRELICENSING AND RESEARCH ACTIVITIES.......... 6
  Activity in Separate Research Facilities.......... 6
  Activity in Licensed Production Facilities.......... 7
RECORD KEEPING AND RECORD RETENTION.......... 7
  Production and Testing Activities.......... 7
  Inventory and Distribution Records.......... 7
ANIMALS.......... 8

SPECIFIC INTERPRETATION OF THE REGULATIONS

A thorough knowledge of both the content and meaning of the Virus-Serum-Toxin Act and the applicable parts of the Code of Federal Regulations are essential for an inspector. Fundamental to the proper interpretation of the regulations are the special definitions given to specific terms in 9 CFR 101.2 through 101.7. When used anywhere in 9 CFR 101 through 117 the special definitions supplant the dictionary definitions. This distinction must be maintained when interpreting findings, and in preparation of reports and communications.

LICENSES AND PERMITS

These documents are basic to the enforcement of the Virus-Serum-Toxin Act. Anyone who imports or distributes any veterinary biological product interstate must hold an unexpired, unsuspended and unrevoked license for both his establishment and for each (at least one) product (102.2).

Establishment License (102.4)	All details of the license must be precisely correct. The location of all veterinary biological production, testing and initial distribution locations must be shown (102.3, 102.4). Each subsidiary and division for which labels are in use must be named on the license (102.3, 102.4). When change of ownership or of controlling interest occurs, a new application must be submitted and the license reissued. (102.3)
Product Licenses	The entire true name of the product and the product code must appear on the license. (102.5) Careful attention should be paid to any additional restrictions or requirements which are listed on the license. Inspection may be the only means of insuring compliance. (102.5) Unless specific action is taken by the Deputy Administrator, products prepared while a firm holds a valid product license may continue to be distributed after termination of that license and until the expiration date of the serial(s) or subserial(s) is reached.
Product License (Special)	Special Licenses are identical to regular Product Licenses except that they always contain special restrictions or requirements and very frequently contain a termination date. The licensee must request reissuance of terminated Special Licenses. (102.6)
Biological Product Permits	Products for research and evaluation (104.4): These permits are almost always issued to allow a single importation. These will ordinarily be encountered when a licensee is conducting research on a new or improved product or evaluating his previously exported product which has been re-entered under permit (104.4) The examination should be conducted to determine whether the permittee has complied with the special requirements and restrictions listed on the permit. Products for distribution and sale: These are essentially the same as a Product License except that they contain an expiration date. The permittee, who must be a United States resident or conduct a business in the United States, is responsible for product storage, distribution, sampling, advertising, label content, and label submissions. (104.5) Products for transit shipment only (104.6); Inspection activities for products imported under these provisions can be conducted without further interpretation of the regulations.

FACILITY REQUIREMENTS (102.3, 102.4, 104.5, 108, 117)

Plot Plans, Blueprints, And Legends	These documents must describe the facilities used in preparation of biological products accurately and completely. All buildings on the licensees premises must be shown in proper reltationship on the plot plan and all boundaries well defined. (108.3) Blueprints must reflect divisions of space as they exist in each building. All means of communication with the outside and between areas inside each building must be shown accurately. Location of each piece of major equipment used in production or testing must be shown or identified by a code which is further described in the legend. Water outlets, drains, and lighting must be shown on the blueprint or described in the legend. (108.4) Plot plan legends describe activities within and the construction details of each building. (108.5) Blueprint legends must accurately describe the activity in each room where biologics are involved including decontamination procedures, and, if appropriate, identify the equipment. (108.5) Facilities, equipment, and management must be appropriate to the stated activities. Location of all microorganisms, stored or used, should be shown, either as part of the pertinent room descriptions or as a supplement to the blueprint legends.
Building Construction	Details must be as shown on blueprints and legends and must be appropriate for the functions performed. (108.8)
Personnel And Product Movement	Room arrangement and management must be designed to prevent comtamination of products and to protect personnel. (108.8) Personnel should be fully informed, preferably by written rules of procedure, of restrictions to traffic which are necessary for protection of product quality. (114.7) The inspector is required to express his opinion on the adequacy and utilization of the space in which the firm's activities are carried out and to make recommendations for corrective measures. No guidelines are possible for this. Reliance will have to be placed on professional judgment developed from training and experience.
Heating, Ventilation, And Plumbing	Design, construction, and use of these utilities must be such that the functions can be carried out with safety to products and personnel. (108.8)
Facilities For Virulent Or Dangerous Organisms	Separate rooms must be used for handling each virulent or dangerous organism and for diagnostic laboratory facilities. (Examples: Rabies fixed and street viruses, anthrax spore challenge, Leptospirae Erysipelothrix, Brucella, *Clostridium botulinum*, *Clostridium tetani* and its toxin, and equine encephalomyelitis viruses). These rooms should be supplied with an air lock and separate air handling system with no return of air to other work areas (108.8, 117.3).
Dressing Rooms, Toilets, And Lavatory Facilities	These facilities must be available and separate from product preparation areas. (108.9)

SANITATION (108.8, 108.10, and 114.7)

There are many variable conditions peculiar to the circumstances of the individual establishment, especially in the matter of sanitation. The measures taken must be appropriate to the need. Special attention should be given to circumstances such as the following:

Rooms where a product in process is exposed must be thoroughly cleaned and decontaminated before beginning work. They must be kept closed during such use. Removal of materials during such operations should be accomplished by use of "pass-throughs".

Animal handlers and caretakers should be prohibited from entering areas where product processing steps are in progress unless they make a complete change of outer garments, including shoes.

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 4
INSPECTION OF ESTABLISHMENTS

INSPECTION OF ESTABLISHMENTS

SUB-UNITS

Page
Preinspection Activities 2
The Inspection Proper 9
Post Inspection Activities 32

PREINSPECTION ACTIVITIES

CONTENTS

TYPES OF INSPECTION 2
- In-Depth 2
- Follow-Up 2
- Special 2

TALLY OF INSPECTIONS 2
THE INSPECTION TEAM 2
- Team Makeup 2
- Team Assignments 3

SCHEDULING AND NOTIFICATION 3
- Scheduling 3
- Notification 3

REVIEW OF AREA OFFICE FILES 4
- Worksheet Used 4
- Establishment License Review 4
- Official Contacts 4
- Principal Officers 4
- Licensed Products Printout 4
- Product Licenses 4
- Product Check-Off Sheet 4
- Permits to Import for Sale 5
- Outline of Production 5
- Labels 5
- Blueprints, Legends, and Plot Plans 5
- Blueprint Checklist 5
- Critical Area Analysis 6
- Water Quality Control 6
- Product Destruction 6
- General Correspondence and Special Files 6
- Product File 6
- Testing Records Printout 6
- Prelicensing/Research File 7
- Product Destruction Records 7
- Past Inspection Reports 7
- Missing Documents 7

PROVIDING FOR EQUIPMENT, LODGING, AND TRANSPORTATION 7
- Equipment Needs 7

SUMMARY 8
- Preinspection Conference 8

PREINSPECTION ACTIVITIES

A good inspection starts by preparing properly before you begin the actual in-plant inspection. At least five things must be considered. First, decide upon the type of inspection. Second, select the inspection team and distribute duties within the team. Third, make up schedules and notify those who need to know about the inspection. Fourth, review Veterinary Services files to gather needed information. Fifth, assemble needed equipment and provide for transportation and lodging needs. Each of these five requirements are further explained in the following pages.

TYPES OF INSPECTION

Each inspection is one of three types: (1) in-depth; (2) follow-up; or (3) special (Ref. VS Memo 800.3).

In-Depth Inspection	An in-depth inspection is a detailed type of inspection in which over-all compliance with regulations and other requirements is systematically examined. The time required for this type of inspection is normally the longest of the three types of inspection. The size of the plant, the number of people in the inspection team, and problems encountered determine the length of time expended. As many inspection categories as possible are examined.
Follow-Up Inspection	Follow-up inspections are made to determine if corrections required as a result of previous in-depth inspections have been made.
Special Inspection	A special inspection is any inspection not of the previous two types. This type of inspection may be requested by either government or industry.

TALLY OF INSPECTIONS CONDUCTED

In the Biologics Program, the number of inspections conducted is one criterion used to evaluate program effectiveness in achieving our objectives. Prompt reporting is therefore important.

Report monthly the number of (1) in-depth, (2) follow-up, (3) special inspections initiated. Report to the Biologics Planning and Analysis Staff through the WBBS. Use the workload and work performed report. (See Figure 4-17).

THE INSPECTION TEAM

The Regional Biologics Specialist serves as the leader of the inspection team and coordinator of the inspection Ref. VS Memo 800.2 III.B.1.(c).

Team Makeup

Team composition and size depends on the size of the plant, the type of inspection, the number and types of products produced, and special problems likely to be encountered.

Identify special problems.

Assign at least one Biologics Compliance Officer to an in-depth inspection.

Arrange to have a Veterinary Services Laboratory (VSL) specialist on the team if testing problems are foreseen. Make request for VSL personnel to the Director, Veterinary Services Laboratories.

Arrange to have a member of Biologics Staff or Field forces on the inspection team whenever advantageous. (Go to Senior Staff Veterinarian or Senior Field personnel.)

Arrange to have VSL Biologics Investigators if the scope or type of inspection requires additional trained personnel of this type. Request as for other VSL personnel.

Attempt to have at least one member of the previous inspection team on the new team. This lends continuity and speeds up the inspection.

Limit the team size to no more than four. Use fewer people if the plant is small or if few products are involved. It may not be necessary to have each team member present for the entire inspection period.

Team Assignments

Tasks related to each of the major categories to be covered in an in-depth inspection are assigned to at least one member of the team at the time the team is formed. Responsibility will normally remain with this assignee throughout the inspection cycle--including writing of the report. Assignments are based upon the training, experience, and expertise of each team member.

Review the categories of inspection.

Set the priorities for categories to be examined during inspection.

Assign tasks to team members.

Record assignments made.

INSPECTION SCHEDULING AND NOTIFICATION

The Regional Biologics Specialist makes recommendations for inspections. The Area Veterinarian in Charge (AVIC) directs and schedules inspections of licensed establishments (Ref. VS Memo 800.2).

Scheduling

Scheduling of inspections really begins some 18 months before the start of the fiscal year when the Regional Directors establish broad inspection goals in cooperation with the Biologics Planning and Analysis Staff and Regional Biologics Specialists. The Regional Directors also request the funds and the manpower needed to accomplish the goals set. As the budget cycle progresses, changes and adjustments are made in the budget. By October 1, when the fiscal year starts, the Regional Biologics Specialist makes more specific plans.

Meet with the AVIC at least once each six months to establish priorities on the inspections that are to be made. Discuss what work should be accomplished and how many man-hours will be needed to do it. Rate priorities as: (1) essential, (2) high priority, but postponable, and (3) omittable with calculated risk to the Biologics program. Take the following into consideration: (1) funds available, (2) people and time available, (3) location of licensee, (4) urgency of need for inspection, (5) interval since last inspection, (6) possible weather or local events problems, (7) activity at the plant, (8) transportation problems, (9) other considerations.

Make team assignments for each inspection.

Write up a tentative schedule based upon your written program. Submit to your Regional Director for his comments and concurrence.

Notification

Notifications are of two types: (1) general and (2) concerning individual inspections.

Prepare notifications of general itineraries monthly. List dates that you will be at various locations but do not publicize exact inspection places by name. Arrange sufficient time for each phase of inspection.

Send this itinerary to your Regional Director(s), AVIC's, Biologics Staff, Regional Biologics Specialists, and Biologics Compliance Officers who need to know.

Prepare notification of the pending inspection of an individual licensee about one month in advance.

Distribute only to the appropriate Regional Director, AVIC, Senior Staff Veterinarians of the Biologics Staffs, the Director of VSL, and other Regional Biologics Specialists. Ask for information or needs that will make the inspection more productive. Include a suspense date for replies.

Notify the firm if it will improve the inspection. If not, maintain security over the dates and location of the inspection so your arrival will be unannounced to the firm.

REVIEW OF THE AREA OFFICE FILES

Area Office files contain a wide variety of material used to prepare for an inspection. Official file documents shall not be removed from the Area Office.

Worksheet

Prepare a suitable worksheet similar to the one shown in Figure 4-1. This worksheet will be used later at the establishment to insure documents in the plant are official.

Establishment License

The establishment license provides the following information for the Worksheet: See Figure 4-3. Note:

1. Firm: the official name of the licensee.
2. Mail address: this is not necessarily the same as the Official Address or the address(es) of the licensed premises.
3. Official Address: note that mail address and firm locations may be different from the official address.
4. Establishment License No.: license number will also appear on test reports, etc.
5. Subsidiaries or Divisions: these are important when labels are checked later.
6. Addresses and locations of licensed premises: these are important later when plot plans are checked.
7. Date of issue: while using the establishment license for worksheet preparation, note the issue date. Compare it with older, obsolete licenses and note recent changes.

Official Contacts

Obtain the following from the Area Office:

1. The phone number for the establishment and closest FTS switchboard number.
2. The official contacts and the alternates for the firm. Area office personnel can find this from the current list supplied by Biologics Licensing and Standards Staff (BLSS).
3. List of the names, degrees, and titles of all the people for which VS Form 14-7, Qualifications of Supervisory Personnel, are on file. See Figures 4-4 and 4-5.
4. Review organization chart if on file.

Principal Officers

Look at the application for establishment license (VS Form 14-1) if on file. See Figure 4-16. Note the principal officers of the organization on the worksheet. This information may be needed when key decisions are made concerning inspection findings.

Licensed Products Printout

Obtain a licensed products printout for the firm. See Figure 4-6. This is produced monthly by the Biologics Data Center. Be sure you have the most recent copy.

Product Licenses

Compare the product license or permit with the printout for each product that is licensed. See Figures 4-6, 4-7, and 4-8. Note any licenses that are not current. Check date issued, true name, and code numbers. Transfer the codes for each product from the product license to the product check-off sheet. See Figure 4-9. Note any restrictions shown on the license.

Product Check-Off Sheet

Fill out a product check-off sheet for each product to be examined. The product license provides the true name, form, and code number for the product and the date the license was issued. The card-size format is useful during later discussions with licensee officials and also for conveniently carrying product information about during inspections.

Permits to Import for Sale

Review the files of permits for distribution and sale. Regulations require that special documents be on file for both the foreign manufacturer and the importer. You are responsible for compliance of the foreign manufacturer importing into your assigned area as well as the importer.

Outline of Production

Remember that disclosure of confidential information contained in an Outline of Production or any other document containing trade secrets to an unauthorized person is a violation of the U.S. Code and may be grounds for fine, imprisonment, or dismissal.

Review carefully the filed Outline of Production and the accompanying VS Form 14-15 Transmittal Form (Figure 4-15). Note the date the outline was approved for filing (stamped). Note recent revisions. These may be pen-and-ink, page, or complete revisions. The outline guides required to organize production outlines are contained in 9 CFR 114.9. An Outline of Production for a product is the best source of comprehensive information on preparation of the product. Note that you may have to go back to an out-dated outline if the product was produced during the time the out-dated outline was current. There is no simple way to demonstrate all the types of information that can be found through a careful review of an outline. Some important parts, however, are:

Parts I-IV (Parts I & II of Allergenic Extracts) which provide detailed information on the processing of the product. Here you will find information that you may want to cross-check with Import Permits for Organisms and Vectors (9 CFR 122), Lists of organisms (9 CFR 114.5), Production Animal Health Records (9 CFR 117.3(b)), Animal Welfare Act Records (9 CFR 1,2,3), preservatives, inactivating agents, etc.

Part VI (Part IV for Allergenic Extracts) provides information on the sampling, packaging, and labeling of a product. It also gives information on storage and initial distribution of a product, plus uses, forms, dosages, expiration date determinations, and related information. You may want to cross-check this information with label lists, sampler reports (VS Forms 14-20 Figure 4-18), inventory records, etc.

The ability to identify and extract useful information from an outline and to use this information effectively in an inspection is a skill that must be continually developed through practice and guidance and the acquisition of new knowledge. Transfer important information to the appropriate product check-off sheet.

Labels

Review the label list and label file. Each licensee is required to submit a list of all approved labels currently being used (9 CFR 112(5)(f)) when VS requests it. This list is submitted to BLSS and a copy is sent to the Area Office. Check that the Outline of Production permits each dosage size for which there is an approved label. Note temporary labels, if any. Put comments on the check-off sheet concerning labels needing special attention. Record trade names on the check-off sheets for convenience later in the plant.

Blueprints, Legends, and Plot Plans

Look at the blueprint and plot plan file. The plot plan shows you the layout of the establishment site. See Figure 4-10. Be sure all buildings for which blueprints are on file are shown on the plot plan. The plot plan legend identifies the buildings and their principal uses. The building blueprints show the layout of the rooms within each building. The blueprint legend identifies pieces of equipment and describes the procedure conducted and the agents that are processed in each room. Identify all automatic controlled equipment to check at the firm. See Figure 4-11. Note filed date of each document and blueprint so as to be sure the Area Office and plant copies are the same. See Figure 4-12.

Blueprint Checklist

Prepare a blueprint checklist for each product. See Figure 4-13. List the code number or agents of each licensed product in the space provided at the left of the checklist. Using the blueprint legend, match the room number with each applicable key operation category that is listed across the top of the checklist. Do this for each product. Be alert for any inconsistencies, such as blocks being blank for certain key operations. Note these and check the production outline to be sure the omissions noted are permissible. If not, note on the worksheet for further attention. This checklist will be very valuable later when products must be traced during the actual inspection.

Analysis to Pinpoint Critical Areas

Analyze the blueprints, plot plan, and legends for the traffic patterns of people, media and glassware movement, provisions for vector control, air flow patterns, sterility or sanitation control, potential cross-contamination. A legend on a transparent sheet which can be placed over the blueprint works well.

Identify locations where contamination might occur; where products or agents might be accidentally mixed or switched; where particularly crucial production steps are carried out. Note these places on the worksheet. Be sure licensed and experimental products can be kept effectively separated.

Water Quality Control Standards Statement

Find the certification on file which shows compliance with applicable water quality control standards. Be sure it is up-to-date.

Product Destruction

Note on worksheets (Figure 4-2) any special product destruction procedures, permitted uses of approved landfills or other information relating to environmental impact.

General Correspondence and Special Files

Go through the correspondence and special files for the licensee. These files contain a variety of information that may further identify items that may need special attention at the plant. Note information pertinent to the inspection. Be sure to verify that the information has not been superseded or countermanded.

Import Permits for Research

Consumer Complaints - List consumer complaints to be discussed with the firm.

Export Certificates

Health Records - Note records that need to be checked at firm such as Brucellosis and E.I.A.

Investigation Reports - Note special investigations of any sort.

Animal Welfare Act - Note if the firm has been exempted from certain requirements by the Deputy Administrator as allowed by 9 CFR 117.1.

Product File

Check the product file. Identifying products that are harmful, dangerous, contaminated or worthless so they will not be marketed is the goal of the Biologics Program. Past test results indicate products that need special attention.

Testing Records Printout

Analyze the licensee's test records, using computer printouts. Look at the computer licensee summary, especially those products that have been unsatisfactory. See Figure 4-14. More recent serials are found in the ledger in the Area Office. Note if VSL, the licensee, or both are finding the unsatisfactory serials. Go to the detailed computer listing to see which specific test procedures are unsatisfactory.

Check the outline and 9 CFR Part 113 to verify the requirements for a satisfactory product. Prepare a tentative list of products that seem to need attention.

Identify tests that VSL is not or cannot conduct on a product for special attention at the firm.

Study specific serial test results in the product file. Select tentative list of serials of product that will be examined in detail. Ordinarily select at least one serial that is nearing its expiration date, at least one that is about halfway through its useful life, and at least one that has been recently produced or is still in process. Add the serial number, trade-name, important points needing special attention, etc. on the worksheet for later use in the plant.

Prelicensing and Research Activities

Familarize yourself with Prelicensing and Research Activities. List the products for which license applications are on file in the Area Office. Note the status of each application. Be sure to note whether blueprint legends have been approved for their preparation in production facilities. Note any special requirements in connection with the prelicensing application procedures. Note any product distribution that BLSS has authorized under 9 CFR 103.

Product Destruction Records

Identify serial lots that should be destroyed. Serials found unsatisfactory by VS testing must be destroyed under VS supervision; other unsatisfactory lots must be destroyed and so certified by the licensee. VS Form 14-45 is certificates showing serial lots destroyed under VS supervision (Figure 4-19). Note serial numbers of lots that should have been destroyed and for which adequate certification should be on file.

Past Inspection Reports

Read previous inspection reports carefully. Previous inspection reports (VS Forms 14-30) and related correspondence contain important information about conditions previously found, especially the one immediately before the present one. Repeat violations of a regulation within 6 months of written notification of the first infraction is prima facie evidence of willful violation, (9 CFR 105.2). Note on the worksheet when and who made the previous inspection, the exceptions found, and corrections that were made. Remember that the letter to the firm is the official notice of non-compliance and should be used as the basis for review.

Missing Documents

Contact the appropriate staff or laboratory unit to arrange for replacing or obtaining copies of any required documents that are missing from Area Office files.

PROVIDING FOR INSPECTION EQUIPMENT, LODGING, AND TRANSPORTATION NEEDS

Your inspections are usually conducted at sites remote from your duty station or the Area Office. You must therefore have: (1) the inspection equipment you need with you; (2) good transportation both to and from and at the site where the inspection will be conducted; and (3) a convenient location apart from the inspection site where private discussions and critiques may be held and preliminary drafts prepared.

Equipment Needs

The following list contains equipment items that may be needed for an inspection:

1. Your badge or valid USDA Identification Card, identification is always required.
2. An electronic calculator for records audit.
3. Thermometers that meet ASTM* accuracy standards for the following applications:

   Sterilizer temperatures around 120° C and 160° C (minimum-maximum needed)**.
   Pasteurizer temperatures around 62° C (if needed).
   Incubator temperatures around 20-25° C and 30-37° C.
   Cooler temperatures around 2-7° C.
   Freezer temperatures around (-7)-(-90°) C.

4. A portable xerographic copier.
5. A camera which utilizes self-developing film.
6. A current set of 9 CFR Parts 101-117 and other policy documents with latest revisions.

*American Society for Testing Materials.

**A suggested source (no endorsement implied) for maximum-minimum thermometers is Brooklyn Thermometer Co., 90 Verde Street, Farmingdale, NY 11735.

7. Blank notebooks, scratch pads and other stationery materials, sets of in-plant worksheets.
8. Reference material prepared during the preinspection period.
9. A copy of this manual.

SUMMARY OF PREINSPECTION ACTIVITIES

Preinspection Conference

When each team member has completed his portions of the Area Office file review and details of scheduling, lodging, transportation, and equipment needs have been arranged, the team leader calls a conference. The following is a checklist for the conference.

Redefine the objectives of the forthcoming inspection.

Review worksheets to insure needed information has been written down and will be available in useful form at the inspection site.

Review schedules, equipment needs, etc.

Answer questions.

Go over final workplan. Be sure everyone is aware and prepared to fulfill his or her role on the Inspection Team.

THE INSPECTION PROPER

CONTENTS

Page

THE INSPECTION PROPER 10
RULES OF CONDUCT 10
ESTABLISHED INSPECTION TECHNIQUES 10
- Audit 10
- Observation 10
- Perambulation 10
- Internal Controls 10
- Worksheets 10
- Formal Reports 11

DIVISION OF RESPONSIBILITIES 11
CONDUCTING THE INSPECTION 11
- Introductions 11
- Initial Meeting 11
- Worksheets 12
- How to Evaluate Exceptions 12
- Types of Exceptions 12
- Categories of Inspection 13
  - Personnel 13
  - Licenses 13
  - Facilities 14
  - Sanitation 15
  - Prelicensing and Research 15
  - Labels 16
  - Virus Seed, Bacterial Stock Cultures, and Cell Lines 16
  - Production Procedures 17
  - Final Production Procedures 18
  - Animals 18
  - Equipment 19
  - Testing Procedures 19
  - Marketing 20
  - Sampling, Consumer Complaints, Product Destruction, Miscellaneous 20
- Categories Cross-Referenced with 9 CFR 101 to 117 21

INSPECTION ROUTINES 27
- Compliance Criteria for Records 27
- Use of Outlines of Production 27
- Routines in the Observation of Production Procedures 28
- Inspection of Controlled Equipment 29

DAILY TEAM REVIEW 30
THE WRAP-UP SESSION 30
GUIDELINES FOR ACTIONS IN SPECIAL CIRCUMSTANCES 31
TEAM WIND-UP MEETING 31

THE INSPECTION PROPER

The biologics inspector must determine that the products have been produced and tested by competent people using acceptable facilities and methods; that products being marketed are not worthless, contaminated, dangerous, or harmful; and that reports and records of production and testing of products are accurate and complete.

RULES OF CONDUCT

Rules of Conduct

The ideal inspector-laboratory relationship is one of mutual understanding, confidence, and respect. Although this ideal cannot always be reached, the inspector should observe these rules of conduct and procedure which will approach the ideal as nearly as possible. Laboratory personnel, generally, are of high caliber, well trained and responsible, and as such are due the consideration and respect of the inspector. There are certain specific rules to be followed by all inspectors.

First, the inspector is in the position of an observer and should in no way assume a note of supervision or enter into operational management.

Second, the inspector should be reasonable in demands on the time of laboratory personnel by limiting questions and conversation to that directly related and necessary to the inspection.

Third, the inspector should not discuss possible exceptions with sub-supervisory laboratory personnel or engage in conversations concerning controversial subjects.

Fourth, the inspector shall be aware that all information obtained is privileged and shall not be conveyed in any manner or form except to those officially authorized by the Deputy Administrator.

Fifth, the inspector should observe all organism and vector control requirements of the laboratory.

ESTABLISHED INSPECTION TECHNIQUES

The following techniques are commonly used in inspection: (1) selective audit, (2) observation, (3) perambulation, (4) evaluation of internal control, (5) completion of worksheets, and (6) issuance of a formal report.

Audit	The inspector picks out certain records for an in-depth review. A trace is then made of related records to establish the validity of the entries on the master records selected. Exceptions are noted.
Observation	The inspector personnally substantiates that information provided VS and records kept by the firm are in agreement with what he finds at the actual situation or site at the establishment.
Perambulation	This is a special class of observations. The inspector unobtrusively watches ongoing operations for sufficient time to observe unusual or uncharacteristic occurrences, especially regarding techniques of manufacture.
Internal Controls	Well-managed enterprises have checks and balances built into their methods of operation to minimize and/or expose errors. The inspector using experience and judgment explores the adequacy of these controls. These findings determine what must be done further to get the information sought.
Worksheets	The inspector himself makes a record of his findings in such a logical and systematic manner that this record may be later admissible as evidence of his audit and findings in a court of law.

Formal Reports The inspector communicates the findings in a written form that can be used later for discussions with supervisors, licensee representatives, other team members, subsequent teams, and others properly authorized to use the information gathered.

DIVISION OF RESPONSIBILITIES

The responsibility of the Biologics Compliance Officer and the Animal Health Technician is to obtain information and report such. The Regional Biologics Specialists and other VMO's obtain information and evaluate the information obtained from the various sources. The team leader evaluates, coordinates, and finalizes the actions that are taken.

CONDUCTING THE INSPECTION

The inspection proper has three phases: (1) an initial meeting with the licensee representative(s) for making introductions, contacts and schedules, and explaining the purposes of the inspection. An initial Administrative review of basic records is also done at this time; (2) the inspection activities themselves; and (3) a wrap-up meeting with the licensee to discuss the inspection findings.

Introductions Do the following upon arrival so senior management officials will know what to expect:

Identify yourself to the licensee's receptionist. A printed card is useful.

Ask for the representative designated to make official contacts with Veterinary Services.

Identify yourself again to the official representative using your badge or ID card. Make this a deliberate act even if you are well known to the representative. Section 157 of Title 5, U.S. Code gives you authority to make the inspection when you have thus shown you are duly authorized.

Inform the licensee representative that you are on the premises to conduct an inspection. Arrange a meeting with the representative, the person-in-charge, and with as many of the supervisory or management staff as he cares to have present at the initial meeting.

Initial Meeting Go over the following points in the initial meeting, being brief, businesslike, and courteous.

State the purpose. Explain what an inspection means. Go over the inspection categories in a general manner.

Develop a preliminary schedule with the licensee. Allocate time for (1) an orientation tour of the facilities; (2) license/blueprints/legends review; (3) a product review (Review of production records can include all records from the acquisition of seed material to the last container of product leaving the plant including operating procedures and records.); (4) an equipment records and equipment operation review; (5) review of experimental, field trial, and consumer complaint records; (6) review of labels and packaging procedures and records; and (7) a wrap-up discussion session.

Discuss VS Biologics Program Inspection Policy. It is:

1. Will go anywhere we feel necessary but will respect licensee policy as far as possible and will not interfere with operations if it can be possibly avoided.
2. Will accept persons to observe and accompany us at any and all times. The firm may designate whomever they wish.
3. Will discuss policy matters only with persons specifically designated by the firm to do this.
4. Will not instruct or admonish any employee.

5. Will discuss findings only with employees that management designates. The items discussed will be repeated to management later.

Discuss what the inspectors need to help them in their inspection.

1. How will inspectors move about the plant?

2. Get names of observers, if any, who will accompany inspectors. Establish ground rules for observers.

3. What are the working hours? Avoid interfering with key personnel at critical times.

4. Obtain a schedule of activities that will be occurring while inspectors are in the plant. This may include:

   (a) filling room schedules
   (b) test starting dates, animal challenge dates, observation times
   (c) inoculation or harvesting schedules

5. Determine the locations where records are kept. This should include the following types of records.

   (a) labels and label files
   (b) animal acquisitions and disposals
   (c) production and testing records
   (d) sterilizer, lyophilizer, and filling records
   (e) outlines of production
   (f) stock culture and master seed records
   (g) distribution records
   (h) inventory records

6. Where may inspectors work? Get working space in a location convenient to the records area and to production and testing facilities, if possible.

Worksheets

The preliminary worksheets prepared during preinspection review are utilized during the inspection proper. Examples of typical worksheets that may be used in the inspection are as follows:

Daily Inspection Notes	Figure 4-21
Additional Daily Inspection Notes	Figure 4-22
Inspection Product Check-off Sheet	Figure 4-23
Additional Product Inspection Notes	Figure 4-24

All worksheets, other notes, exhibits, employee statements become part of the inspection report. These must be usable as supporting evidence for all exceptions noted.

Make notes legible, clear, and preferably indelible.

Cross-index or number so sequences can be maintained and any omissions made apparent.

Identify by date and by person preparing.

How to Evaluate Exceptions

There are three types of exceptions: (1) Minor, (2) Less Serious, and (3) Serious.

Types of Exceptions

Minor exceptions are not apt to affect quality of product but indicate laxity or error that could become more serious if not corrected. If numerous minor exceptions are noted during the inspection, it is indicative of poor management and should be considered as having cumulative effect.

Less serious exceptions by repetition or very nature may affect quality of a product. They may require evaluation at the Area Office before final action is taken.

Holding release of serials or products may be required.

Serious exceptions. Violations of this degree will probably affect the quantity of the product or products or may be willful. This type of violation will require more thorough documentation and referral to higher authority. Either stop sale or temporary suspension of license should be considered.

Each exception must be related to the Virus-Serum-Toxin Act or to the regulations issued persuant to the Act. An inspector must not go beyond this authority and should develop the habit of carefully determining what regulations might be violated when a possible exception is noted. This will insure two things: (1) that the inspector has not exceeded his authority and (2) that the inspector will be continually increasing his effectiveness.

Categories of Inspection

A guide to inspection has been prepared and divided into fourteen major categories. These categories are used to assign inspection work and as a format for the final summary VS Form 14-30 Inspection Report (Figure 4-31). Listed under each category is a checklist of audit and observation items that the inspector should consider. These checklists are not to be considered limiting or all inclusive but as a guide to examining the major categories.

I. Personnel

A. Audit

1. Compare the firm's VS Form 14-7 file with your preinspection work list for any unreported changes in key personnel, deletions, additions or job changes or request the official in charge to certify your preinspection list is correct. Recertify official contact and alternates.

2. Review the firm's system for keeping the VS Form 14-7 file up to date. Identify person responsible for making periodic reviews.

3. Obtain a current firm organizational chart. If not available, obtain the information necessary to allow you to establish official lines of responsibility for the firm, especially relationships among production, testing, and marketing.

4. Determine if job titles accurately reflect job responsibilities.

5. Determine who supervises the care and welfare of animals and what veterinarian determines health of admitted animals.

B. Observations

1. Observe operations to determine if employees are adequately trained and supervised so as to be competent in good laboratory techniques. Observe if they follow lines of responsibility noted on the organization chart.

2. Notice if there is an adequate number of personnel; if employees are observing in-house rules; their general attitude toward their work.

3. Be aware of personnel health conditions that might affect the product.

II. Licenses

A. Audit

1. Compare firm's copy of Establishment License with your preinspection notes. Review with official in charge ownership, parent company, subsidiary and division relationships. Verify that addresses, locations, and other information shown on the license are correct.

2. Verify that the firm's file of Product Licenses contains the same information found on preinspection. Discuss activity of each product with the official in charge. If the product is not being produced, the firm may wish to return the license to VS for termination.

3. Note which Product Licenses expire or have special requirements. Remind firm of expiration dates. Determine if special requirements have been met or are being perused.

4. Note special requirements on Permits to import products for sale. There are special regulations covering the foreign manufacturer, the importer (permittee), sampling imports for VS, and handling unsatisfactory serials. Be sure copies of required documents are on file. Permits expire.

5. Check Permits to import products or organisms for research and evaluation issued to this licensee as noted on your preinspection list. Ask for any additional ones the licensee may have. Check for compliance with special requirements listed on the Permits and with the regulations covering importation for research. Permits expire.

B. Observations

1. Note location of all buildings, appurtenances and equipment used to produce, test, and store products to be sure that all premises are properly identified on the Establishment License. Note any indication of change in ownership, location, or operation of the establishment.

2. Verify that all products observed in production or testing on licensed premises are covered under a valid Product License or are otherwise permitted.

3. Observe for compliance with special requirements of Permits to import product for sale.

4. Inspect facilities and conditions where Permit imported research material is handled to be sure it meets requirements. Observe for any other imported biologics on licensed premises. Biologics exported from the U.S. may only be returned by Permit for research.

III. Facilities

A. Audit

1. Inspect all premises against the appropriate plot plan and legend for accuracy.

2. Compare facilities against the blueprints for evidence of unreported remodeling, new major equipment, relocated key items and other discrepancies. Refer to exceptions in preinspection notes.

3. Check that legends showing special use facilities such as public diagnostic clinic, separate and appart research areas, pharmaceutic production, are correct. Determine location of isolation facilities for in-coming animals if required.

B. Observations

1. Observe the arrangement and construction of the facilities. Determine if this arrangement provides adequate and appropriate isolation for each product.

2. Verify that the actual use of production and testing rooms is as reported in the blueprint legends. Evaluate this use for possible adverse affect on the product.

3. Verify that construction and finish of all areas relating to preparation of biological products, are such that they may be thoroughly cleaned.

4. Observe that lights, ventilation systems, heating and cooling systems, hot and cold water supplies, and drainage systems are adequate and functioning.

5. Observe traffic patterns through production areas. Check enforcement of movement restrictions. A restricted area should be posted.

6. Evaluate adequacy of available space.

7. Observe that dressing rooms, toilets, and lavatories are appropriately placed, sufficient in number, and separated from production. Soap, towels, and hot water should be available.

IV. Sanitation

A. Audit

1. Verify that sanitizing is done in rooms--when and where required as described in legends and Production Outlines. Determine if appropriate chemicals are being used.

2. Compare procedures with the weekly or daily schedule of operation.

B. Observations

1. Notice if outside premises are properly drained, clean, and orderly as required and are free from accumulated trash or construction debris. No nuisance is allowed.

2. Note whether a conscientious effort is being made to control vermin, especially in animal quarters.

3. Check disposal methods for all wastes from firm--trash and debris, sewage, biological wastes.

4. Observe inside premises for clutter, lack of removal of unused equipment, dirt, etc., particularly in areas related to production and in high traffic areas.

5. Note accumulation of unnecessary material in coolers, production area, lab rooms, etc.

6. Notice whether all personnel including maintenance people who enter production areas are wearing acceptable clean laboratory clothing. Note if special clothing requirement areas are posted and requirements enforced by the licensee.

7. Observe for unsanitary practices by employees.

V. Prelicensing and Research Activities

A. Audit

1. When research is conducted in production facilities, BLSS gives permission and sets any special requirements. Examine records to confirm that such restrictions are being complied with.

2. Verify that required records relating to prelicensing products are being accurately maintained.

3. Check records for proper disposal of animals in which experimental products have been used.

4. Differentiate between research being conducted using organisms related to previously licensed work with new organisms not related to licensed product. Complete records are required for both but restriction can be less for related organisms.

5. Review field trial records for compliance with special restrictions and requirements.

6. Some organisms related to licensed product but not approved for use in licensed product may be maintained--check records for permission, methods of maintenance and security.

B. Observations

1. Verify the separation of personnel, supplies, and equipment between research and production.

2. Observe the in-house controls on movement of personnel, supplies, and equipment--between research production and testing areas.

3. Check for production related testing in research areas.

4. Check disposal methods for research material.

5. Observe specific research or pre-licensing activities on request from BLSS.

VI. Labels

A. Audit

1. Check the files of the firm's label controller for inactive, superseded, or obsolete labels noted during your preinspection review.

2. Labels for autogenous bacterins have special requirements. Determine compliance.

3. Determine how and by whom expiration dates are assigned.

4. Determine how label control person knows when a new label has been approved.

5. Check the label stock against label file for accuracy. Determine if a stamped copy of approval labels are readily available to person issuing labels.

6. Accountability must be maintained for all labels printed for use on licensed product. Check inventories, use records and labels damaged or destroyed. Determine how the firm accounts for roll labels and if actual inventories are made.

7. Check stock labels for distinct variance in color, style, printing changes, etc. from approved labels.

B. Observations

1. Check that labels are not left unattended where they could be pilfered or inadvertently used on wrong product. Determine if imprinted roll labels are voided at end of run.

2. Check security of labels in storage. Remember cartons and enclosures too.

3. Observe by whom and when imprinted serial numbers and expiration dates are inspected.

VII. Virus Seeds, Bacterial Stock Cultures, and Cell Lines

A. Audit

1. List Virus Seed, Bacterial Stock Culture, and Cell Line records you reviewed. Note which are on Master Seed concept.

2. Check the records of each seed or culture passage level, determining if each conforms to the outline of production. Check for accountability and identification, tracing seed or culture from aquisition to production of serials. Identify tests to check later.

3. Cells have very specific requirements for maintenance. Check the records for accountability and identification. Trace back to acquisition and forward to production. Note tests to check later.

4. Determine where cells, seeds, and cultures are maintained, handled and produced, and cross check with blueprint legends.

B. Observations

1. Check any production or testing procedures in progress for compliance with the outline or regulations. Note regularity of virulence checks,

methods of maintenance, frequency of passage, storage, current inventory, etc.

2. Observe methods of maintenance, storage and inventory of seeds, cultures, or cells.

3. Check for separate storage facilities for virulent or dangerous microorganisms.

VIII. Production Procedures

A. Audit

1. List serials and bulk lots examined, noting which were checked by observation or record, or both.

2. Review selected serial assembly records against the appropriate outline. These should include complete identification of all added ingredients and account for each step in final processing through completion of the bulk serial. Observe for losses or gains in volume, actual or estimated measurements, authentication of critical steps, and identification of the operator. Identify each bulk lot, raw ingredient, major equipment, procedure, or test. Certify the procedures against the outline at this point. Determine if major equipment is identified and has been properly sterilized. Hold other identified items for checking later.

3. Review the selected bulk lot or batch records of raw biologics and compare each step against the outlines. Determine record keeping compliance. Trace back to appropriate seed or culture and forward to the serial assembly. Identify all ingredients, cell cultures, and tests for later checking.

4. Review selected ingredient records against the outline, special outline, or standard laboratory procedure. Note record keeping compliance. Identify tests run and raw materials used. Be sure to note special requirements for certain ingredients, e.g. E.I.A. test for horse serum.

5. Review selected cell culture production records against outline and regulations. Identify raw materials and tests run. Note record keeping compliance.

6. Review selected diluent production records for compliance.

B. Observations

1. Check any production procedure in progress for compliance with the production outline and blueprint legends.

2. Identity of in-process material must be maintained. Note the manner of identification used and consistency of use, e.g.: color coding, lot numbers, product name.

3. Observe whether proper laboratory techniques and sterile practices are followed by laboratory personnel when required.

4. Observe operations in the media kitchen.

5. Determine if unauthorized reprocessing is being conducted--further procedures on a serial of liquid product after bulking and identification, other than filling, and labeling, not authorized in the outline.

6. Note variations in procedures which differ from the outline of production and evaluate effect on product. Even though the procedures may be within limits of acceptable laboratory practice or are intended to improve the product, they are not allowed unless the outline is changed correspondingly. Determine if approved outlines are available to and used by line supervisors.

7. There are numerous details of production procedures that may affect the quality of a product not noted above. Knowledge of biological production will make the inspector aware of them.

IX. Final Production Procedures

A. Audit

1. Check filling records for recorded losses or gains, fill checks, and filling problems. Determine the firm's standard fill range and the maximum-minimum range for each fill size. How are excessive or low filled vials handled. Is there a written policy.

2. Determine the lyophilization requirements for each product. Review selected serial lyophilization records for compliance and record keeping requirements.

3. Controlled freezing is also critical for products such as Marek's Disease Vaccine. Check records for correlation with the outline.

4. Finishing constitutes handling of a serial from filling through packaging. Losses incurred through breakage, loss of vacuum, etc. must be noted in the serial records.

5. Determine if a copy of the imprinted label, carton and the enclosure are attached to the serial record.

B. Observations

1. Observe and evaluate actual filling procedure, methods for aseptically handling material, conduct of necessary fill checks, proper mixing during fill, and availability and use of worksheets. Determine if employees know the fill limits and how to handle unacceptable filled vials. Observe if fill limits are posted.

2. Check lyophilization procedures such as stoppering devices, use of one or more compressors, mixed container sizes on one unit, shelf variations.

3. Note in-house vial and label inspection procedures, sampling, identification of unlabeled vials, and who controls product until released.

4. Check handling of diluent, how and where is it stored, how it is accounted for.

5. Check freezing procedures. Note time elapsing from filling to start of freezing and rate at which product temperature is lowered.

6. Observe several selected serials for product uniformity, color, volume, texture, capacity, labeling, packaging, readable serial number and expiration date, and Markem or silk screen rub off.

X. Animals

A. Audit

1. Check procurement and pre-purchase test records on animals used in production and testing for completeness, accuracy, and for compliance with outline requirements and Animal Welfare regulations. Review the health status report by admitting veterinarian. Where required, proper health certificates must have been issued and filed--example: E.I.A. testing records.

2. Check preinspection notes and with licensee for Deputy Administrator exemption from the Animal Welfare Act.

3. Records must be complete for animals used in production or testing and are examined as part of Categories VIII and XII.

4. Determine if the firm keeps accurate records identifying and accounting for final disposition. Certain animals must be quarantined before remove and must be moved with the appropriate forms.

B. Observations

1. Check for compliance with requirements of the Animal Welfare Act. Animals not subject to the Act should also be cared for in the spirit of the Act unless specifically exempted by the Deputy Administrator.

2. Note whether animals are adequately identified.

3. Determine if a firm has post mortem facilities for animals used for production and test purposes.

4. Determine if the admitting veterinarian examines the animals before admittance or in a separate quarantine area on premises. Note if another employee examines for the veterinarian.

5. Observe for preconditioning, treating, or inoculating animals so as to adversely affect testing or production.

XI. Equipment

A. Audit

1. Identify from your preinspection list the automatically controlled equipment, environment rooms, and other major specialized equipment used in production, testing, and storage of product. Certify location against the blueprint legends.

2. List equipment or rooms checked, location, and whether checked by record review, observation or measurement with VS standard devices.

3. Review records of automatically controlled equipment and determine if it is being operated according to regulations and outlines. Is record keeping in compliance.

4. If firm is exempted from the required automatic controls and recorders on certain equipment, does the system in effect provide the required information and control.

5. Determine standardizing system used and records kept by the firm to insure that automatically controlled equipment and environmental rooms are operating properly.

B. Observations

1. Check for major specialized equipment or environmental rooms not listed on the blueprint legend and determine if they are being used in production, testing, or storage of product. Determine compliance.

2. Observe operation of automatically controlled equipment and environmental rooms and determine if they are being operated properly by the firm.

3. Measure and record temperatures with standard VS thermometers and compare with firm recording devices.

4. Note if all major equipment is uniquely marked so it may be identified in the records (assuming there is more than one).

XII. Testing Procedures

A. Audit

1. List product, serial or lot number, and whether the test was reviewed by records or observation.

2. Records of testing done as required by outline of production or regulations must show when observations are made and must be authenticated by the individual making the observations. Evaluate for evidence of "Dry-Labbing". Review previously selected test records of ingredients, bulk lots, serials, seed, cultures, cell lines, and diluents for compliance.

3. Note if proper controls are listed for each test group, if appropriate tests were run on the test media or animals, and if equipment was providing the required environment for the test.

4. Make sure that all tests summarized on VS Form 14-8 reports are supported by daily records.

5. Review any tests conducted by the firm that are not reported on the VS Form 14-8. Determine whether or not these results indicate that the product may require special attention.

6. In those instances where retests are permitted by regulations or the outline of production, evaluate for validity.

7. Identify tests VSL cannot run, from the preinspection notes. Audit records of as many as possible.

8. Certain organisms not named in the outline of production are necessary to testing cycles. These should be listed in the blueprint legend.

B. Observations

1. Observe testing procedures and determine if they are in compliance with the outline of production and the regulations: Give special attention to tests that VSL cannot confirm.

2. Observe testing procedures and determine if proper lab technique is being employed along with proper recording.

3. Observe if proper testing controls are used.

XIII. Marketing

A. Audit

1. Evaluate the method of reconciling estimates and actual inventories.

2. Determine whether distribution records are adequate for inventory control.

3. Determine if the firm's records are such that a total stop sale or recall down to user level could be carried out by the firm should it become necessary.

4. Note if products are being distributed in accord with special license or state requirements.

B. Observations

1. Evaluate the physical system of control and identification on pre- and post-release serials. The system should prevent inadvertent distribution of unreleased serials.

2. Verify the accuracy of marketable inventory as reported on VS Form 14-8. Request the licensee to report major change in inventory.

3. Check if cooler space is adequate for licensed products at the normal level of production.

XIV. Sampling, Consumer Complaints, Product Destruction, Miscellaneous

A. Audit

1. Discuss firm's consumer complaints with the responsible official. Review the complaint files as indicated in your preinspection notes or as required by license provision.

2. Examine preinspection production destruction notes--verify that products found unsatisfactory by the firm are reported destroyed on a VS Form 14-8.

3. Review for accuracy the production summary forms the firm presents to the sampler.

4. Check that products "to be destroyed under VS supervision" have been properly quarantined and destruction conducted with VS personnel observing and have been subsequently reported on VS Form 14-45. Identify quarantine area on the blueprint. Check inventory and accounting of any retained samples from unsatisfactory serials.

5. Check the legends for notation of storage of reserve samples.

B. Observations

1. Inspect storage areas to verify products reported destroyed by firm are not still being retained by the firm.

2. Inspect the quarantine area for security.

3. Review sampling techniques with sampler and firm. Be sure samples collected are representative. Check the methods of authentication, modify if necessary. Check the method of packing samples for shipment. Review VS Form 14-20 preparation with sampler. Insure that the sampler is provided with and uses appropriate protective clothing.

4. Review product destruction techniques with the sampler and the firm.

5. Check reserve samples for proper authentication and security.

CATEGORIES CROSS REFERENCED WITH 9 CFR 101-117

I. Personnel	(a)	Designation of Official Contact with VS	114.7(a)
	(b)	Education and Training - VS 14-7 File	104.5(a)(3) 114.7(b)
	(c)	Demonstrated Fitness/Competency	102.4(b)(2) 104.5(a)(3)
II. Licenses	A.	Establishment License	
	(a)	Definitions	101.2(q)(r)(s)
	(b)	Application For	102.3(a)(1)
	(c)	Conducting More Than One Establishment	102.3(a)(2)
	(d)	Operation of Subsidiaries	
		1. Definition of Subsidiary	101.2(k)
		2. Permission to Operate	102.3(a)(3)
	(e)	Product License Application must Accompany Establishment License Application	102.3(a)(5)
	(f)	Change of Ownership, Operation, or Location	102.3(a)(6)
	(g)	Prerequisites to License Issuance - Prelicensing Inspection Required	102.4
	(h)	Suspension or Revocation of License	105.1(a)
	(i)	Separation of Establishments	114.3(a)
	(j)	Rights to Inspect Establishments	115.1
	B.	Product License	
	(a)	Definitions	101.2(t)(w) 101.3(a)
	(b)	Types of Products	101.3(b) to (g)
	(c)	Application For	102.3(b)
	(d)	Prerequisites to License Issuance	102.5, 102.6
	(e)	Suspension or Revocation - Hearing Required	105.1(a)
	(f)	Suspension or Revocation - Dangerous Product	105.3
	(g)	Termination for Inactivity	105.4
	(h)	Joint Production by Licensee/Subsidiary	114.16

(i)	Right to Inspect Products	115.2
(j)	At Least One Product License Other Than Autogenous Biologic Required	102.4(f)

C. Product Permit

(a)	Definitions	101.2(n)(v)
(b)	Application For	104.3
(c)	When Permit Required	104.1
(d)	Types of Permits	104.2
	1. Research and Evaluation	104.4
	2. Distribution and Sale	104.5
	3. Transit Shipment	104.6
(e)	Permits Expire	104.7(c)
(f)	Illegal Imports	104.8(a)
(g)	Imported Products Found Unsatisfactory	104.8(b)
(h)	Suspension or Revocation - Hearing Required	105.1(a)
(i)	Suspension or Revocation - Dangerous Product	105.3
(j)	Right to Inspect Products	115.2
(k)	Right to Inspect Foreign Facilities - Written Authorization on File	104.5(a)(2)
(l)	Determination of Condition of Equipment/Facilities Required - Producer, Importer or Both	104.2(c)
(m)	Conditions for Re-Entry of Exported Product Under Permit	104.4(d)
(n)	Right to Inspect Permittee Facilities	104.5(b)(1)
(o)	Sampling Imports	104.5(b)(4)

III. Facilities

(a)	Rights to Inspect Facilities	115.1 102.4(a)
(b)	Definitions	101.2(p)
(c)	Plot Plans/Blueprints to Accompany License/Permit Application	102.3(a)(4) 104.5(a)(1)
(d)	Legends Required	102.3(b)(2)(iii)
(e)	Satisfactory Facilities Required for License/Permit	102.4 104.5(b)(1)
(f)	Research Facilities Separate and Apart	103.1
(g)	Defective Construction Grounds for License Suspension/Revocation	105.1(a)(1)
(h)	Plot Plans/Blueprints/Legends	108.2 to 108.7
(i)	Construction of Building	108.8
(j)	Dressing Rooms and Other Facilities	108.9
(k)	Outer Premises and Stables	108.10
(l)	Water Quality Requirements	108.11
(m)	Separation of Establishments	114.3(a)
(n)	Storage and Handling	114.11
(o)	Animal Facilities	117.2

IV. Sanitation

(a)	Outer Premises Clean and Orderly without Nuisances	108.10(a)
(b)	Stables/Animal Quarters Kept Sanitary	108.10(c)
(c)	Establishment Free of Flies, Rodents/Other Vermin	108.10(c)
(d)	Refuse Disposal in Conformance with Local Health Practices	108.10(c)
(e)	Due Sanitary Precautions/Good Sanitary Measures to be Practiced	114.7(c)
(f)	Clean Clothing to be Worn in Lab Rooms	114.7(c)(1)
(g)	Unsanitary Practices Prohibited	114.7(c)(2)
(h)	Conditions for Disposal of Unsatisfactory Products/By-Products	114.15
(i)	Disposal of Animals and By-Products VS Memo 800.56	103.2
(j)	Proper Ventilation to Insure Sanitary Conditions Required	108.8(d)

V. Prelicensing and Research Activities	(a)	Definitions	101.2(o) 101.3(b)
	(b)	State Permissions	103.3(a)
	(c)	Research Data/Test Reports Required to Support Product License/Permit Application	102.3(b)(2)(ii) 104.5(a)(5)
	(d)	Permission to Prepare Experimental Products on Licensed Premises Required	103.1
	(e)	Exemptions if Research Facilities Separate and Apart	103.1
	(f)	Requests to Remove Animals	103.2
	(g)	Disposition of Animals Given Experimental Products	103.2
	(h)	Distribution of Experimental Products	103.3
	(i)	Field Trials	103.3
	(j)	Prelicensing Inspection Authorized	102.4(a)
	(k)	Permit Requirements for Import of Products Involving Research/Evaluation	104.4
	(l)	Label Requirements for Import of Products for Research/Evaluation	112.9
	(m)	Products Not Prepared Under License	114.2
	(n)	Micro-organism Control	114.5
	(o)	Conditions for Maintenance of Diagnostic Facilities	117.3(e)
VI. Labels			
	(a)	Definitions	101.4
	(b)	Labels/Sketches to Accompany Product License/Permit Application	102.3(b)(2)(iv) 104.5(b)(3)
	(c)	Imports	104.4(c)
	(d)	Assurance Not to Mislead/Deceive Filed with Establishment License Application	102.4(b)(3)
	(e)	Labels/Sketches to Accompany Requests to Distribute Experimental Products	103.3(d)
	(f)	Misleading/Deceptive Labeling Grounds for License Revocation/Suspension	105.1(a)(3)
	(g)	General Requirements for Labeling and Packaging	112.1 to 112.10
	(h)	Advertising Claims	104.5(b)(2) 102.4(b)(3)
	(j)	In-Process Tags	114.4
	(k)	Expiration Date Determination	114.13
	(l)	Extension of Expiration Date	114.14
	(m)	Label Records	116.3
VII. Virus Seed, Bacterial Stock Cultures, and Cell Lines	(a)	Definitions	
		1. Cell Cultures	101.6
		2. Seed Virus	101.7
		3. Organisms and Vectors	122.1
	(b)	Permit Required to Import/Transport Organisms or Vectors	122.2 to 122.4
(c)	(c)	Separate Rooms/Compartments Required for Handling Storage of Virulent or Dangerous Micro-organisms	108.8(c)
	(d)	Complete Record of Micro-organisms Used Required	114.5
	(e)	Micro-organisms to be Free of Causative Agents of Other Diseases	114.5
	(f)	Identification of Micro-organisms Required	114.9
	(g)	Inspection of Organisms/Vectors Authorized	115.1
	(h)	Exemption to Animal Testing if Master Seed Virus is Approved	113.8
	(i)	Requirements for Cell Cultures	
		1. Primary Cells	113.51
		2. Cell Lines	113.52
	(j)	General Requirements for Master Seed Viruses	113.135(a) to (c)
	(k)	Master Seed Concept	101.7

VIII. Production Procedures	(a)	Definitions	101.3
	(b)	Adequate Methods of Product Preparation Necessary for Product License/Permit	102.4(b)(1) 104.5(a)(2)(3)
	(c)	Products must be Prepared in Accordance with Regulations and Outline - No Change Without Prior Approval	102.5(d)(1) 104.5(a)(4)
	(d)	List of Licensed Products to be Continued in Production Required upon Request	102.5(d)(3) 114.8(e)
	(e)	Faulty Methods of Preparation Grounds for License Revocation/Suspension	105.1(a)(2)
	(f)	Ingredient Requirements	113.50 to 113.54
	(g)	General Product Requirements	114.1
	(h)	Product Not Prepared Under License Non-Marketable	114.2
	(i)	Provisions for Movement of Product Between Licensed Establishments	114.3(c)(d)
	(j)	Proper Identification of Products Required	114.4, 114.6
	(k)	Thorough Mixing of Liquid Products Required	114.6
	(l)	Outlines of Production Required	114.8
	(m)	At Least Annual Review of Each Outline Required	114.8(d)
	(n)	Outline Modifications can be Required to Eliminate Government Objections	114.8(f)
	(o)	Outline of Production Format Guidelines	114.9
	(p)	Antibiotics as Preservatives	114.10
	(q)	Requirements Governing Rebottling	114.17
	(r)	Requirements Governing Reprocessing	114.18
	(s)	Inspection of Methods of Manufacture Authorized	115.1
	(t)	General Record/Reports Requirements	116.1(a) 116.5
IX. Final Product Procedures - Filling, Lyophilization, and Finishing	(a)	Definitions	101.3(c) to (e) 101.3(h),(i) 101.4(b),(e)
	(b)	Adequate Storage Required for Products Imported under Permit	104.5(b)(1)
	(c)	Packaging Desiccated (Lyophilized) Products	112.6
	(d)	Packaging Requirements for Product Produced for Export Only	112.8
	(e)	Outline of Production to Contain Special Packaging Requirements	112.10
	(f)	Thorough Mixing Required During Bottling	114.6
	(g)	Outline of Production Format Guidelines Post-Preparation Steps	114.9
	(h)	Storage and Handling	114.11 114.13(b)
	(i)	Requirements for Joint Licensee/Subsidiary Product Production	114.16
	(j)	Storage Records	116.2
X. Animals	(a)	Definitions	101.2(c) 101.5(i),(j) 122.1
	(b)	Disposition of Animals Given Experimental Product/Live Organisms	103.2
	(c)	Data Required to Show Experimental Product will not Cause Unwholesomeness	103.3(f)
	(d)	Statement Required Prior to Movement of Experimental Product Test Animals	103.3(g)
	(e)	Permit Required to Import/Transport Vectors	122.2
	(f)	Requirements for Stables/Animal Rooms	108.10
	(g)	Authority to Inspect Vectors in Establishment	115.1
	(h)	Animal Records	116.6

	(i)	Use of Animals Must Meet Animal Welfare Act Standards	117.1
	(j)	Animal Facilities	117.2, 108.10
	(k)	Admittance of Animals	117.3
	(l)	Identification of Animals Required	117.3(c) 117.4(b)
	(m)	Health Surveillance of Test Animals Required	117.4(a)
	(n)	Conditions for Preconditioning/Treatment of Test Animals	117.4(c)
	(o)	Segregation of Test Animals	117.5
	(p)	Removal of Production or Test Animals from Premises	117.6
XI. Equipment			
	(a)	Definitions	101.2(p)
	(b)	Equipment Inspection Required Before Establishment License/Permit Issued	102.4(a) 104.2(c)
	(c)	Important Stationery/Other Essential Equipment Must Be Identified on Blueprint/Legend	108.4(f) 108.5(b)(2)(3)
	(d)	Equipment Sterilization Requirements	109.1
	(e)	Sterilizers Must Have Recorders/Other Approved Systems	109.2
	(f)	Pasteurizer Requirements	109.3
	(g)	Provisions for Completion of Product when Essential Equipment Fails	114.3(c)
	(h)	Thorough Mixing Required During Bottling	114.6
	(i)	Inspection of Equipment Authorized	115.1
	(j)	Requirements for Sterilization and Pasteurization Records	116.4
XII. Testing Procedures	(a)	Testing Terminology	101.5
	(b)	Definitions - Biological Products and Related Terms	101.3
	(c)	Definitions - Cell Cultures	101.6
	(d)	Definitions - Seed Virus	101.7
	(e)	Purity/Safety/Potency/Efficacy Test Reports Must Accompany Product License/Permit Application	102.3(b)(2)(ii) 104.5(a)(5)
	(f)	Every Serial/Subserial Manufactured/Imported Must Be Tested	113.1
	(g)	Testing Aids Available	113.2
	(h)	Sampling of Biological Products	104.5(b)(4) 113.3 114.8(e) 114.17(d)
	(i)	Exemptions to Tests	113.4
	(j)	Product Cannot Be Marketed Prior to Being Found Satisfactory by All Tests	113.5(a)
	(k)	Competent Employer Must Observe All Critical Periods of Tests	113.5(b)
	(l)	Test Records Required	113.5(c) 116.7
	(m)	Definition of "No Test"	113.5(d)
	(n)	Upon Approval, Use of New Test Methods Mandatory	113.5(e)
	(o)	VS Testing Authorized, No Marketing Permitted Until VS Tests Completed	113.6(a)
	(p)	Product Cannot Be Released if Found Unsat By Testing	113.6(b)
	(q)	Testing of Products with Multiple Fractions	113.7
	(r)	Virus Titrations Permitted in Lieu of Animal Tests If Approved Master Seed Used	113.8
	(s)	Potency Test Confidential Until at Least Three Licenses Have License For Product	113.9
	(t)	SR Test Must Be Used Unless Given Specific Exemption	113.9(b)
	(u)	Conditions for Testing Bulk Material for Export Only	113.10
	(v)	Standard Testing Procedures	113.25 to 113.41
	(w)	Ingredient Requirements	113.50 to 113.54
	(x)	Testing Requirements for Live Bacterial Vaccines	113.65 to 113.67

	(y)	Testing Requirements for Inactivated Bacterial Products	113.85 to 113.106
	(z)	Testing Requirements for Killed Virus Products	113.120 to 113.129
	(aa)	Testing Requirements for Live Virus Vaccines	113.135 to 113.165
	(bb)	Testing Requirements for Diagnostics and Reagents	113.200 to 113.202
	(cc)	Testing Requirements for Blood Origin Products	113.250 to 113.255
	(dd)	Micro-organisms Used in Preparation of Product Must Be Free of Causative Agents of Disease	114.5
	(ee)	Outline of Production Format Guidelines for Testing Requirements	114.9
	(ff)	Conditions for Use of Antibiotics as Preservatives	114.10
	(gg)	Authority to Inspect Products/Methods in an Establishment	115.1
	(hh)	Requirements for Handling of Test Animals	117.4, 117.6
	(ii)	Reporting to VS All Tests Conducted Required	113.5(c)
XIII. Marketing			
	(a)	Definitions	101.2(l) to (n) 101.3(e) 101.4(c)
	(b)	Assurance Required That Advertising/Market Containers Will Not Mislead/Deceive	102.4(b)(3)
	(c)	Product Distribution Must Comply with State Laws	102.5(d)(2)
	(d)	Conditions for Distribution of Experimental Product	103.3 112.9
	(e)	Exported Product Not Ordinarily Allowed Re-entry to U.S.	104.2(d) 112.8(a)(2)
	(f)	Illegal Shipments	104.8
	(g)	Misleading/Deceptive Advertising or Labeling Grounds for License Revocation/Suspension	105.1(a)(3)
	(h)	Willfulness/Public Health, Interest, or Safety Grounds For Informal License Suspension	105.1(b)
	(i)	Repeat Violation within 6 Months Primafacie Evidence of Willfulness	105.2
	(j)	Stop Sale of Dangerous Product Permitted Pending Formal Proceedings	105.3(a)
	(k)	Stop Sale of Products Found Unsatisfactory by Part 113 Permitted	105.3(b)
	(l)	False/Misleading Label/Stamp/Mark on Carton/Final Container Not Allowed	112.1(a)
	(m)	Altering/Marking/Removing of Label Not Allowed	112.1(b)
	(n)	Label Legibility Throughout Dating Required	112.1(c)
	(o)	Label Requirements for Distributors	112.4(b)
	(p)	Label Requirements for Products for Export Only	112.8
	(q)	No Product Not Prepared Under License Shall Be Shipped	114.2(a)
	(r)	Storage and Handling Requirements	114.11
	(s)	No Extension of Dating Permitted if Product Has Left Premises	114.14(a)(2)
	(t)	Inspection of Licensed Product Authorized at Any Time Or Place	115.2
	(u)	Sale/Barter/Exchange of Worthless/Contaminated/Dangerous/Harmful Product Prohibited Upon Notification	115.2
	(v)	Inventory and Distribution Records Required	116.2
XIV. Sampling, Consumer Complaints, Product Destruction, Miscellaneous	(a)	Miscellaneous Definitions	101.2, 1.1 122.1
	(b)	Rules for License Revocation/Suspension	123
	(c)	Written Notification of Infractions Required	105.2, 105.3
	(d)	Completion and Retention of Records	116.8
	(e)	Sampling Authorization	113.8-104.5(b)(4)
	(f)	Sampling Imports	104.5(b)(4)

INSPECTION ROUTINES

Use of a pre-planned routine to gather information on the compliance status of specific items or procedures is your best assurance that you will discover the information you want. There is no way all the routines that you may need can be described. The following, however, are several routines of major importance covering the areas of records, products, production procedures, and controlled equipment. During the course of use of these pre-planned routines, it is almost certain that you will discover items that need further comprehensive investigation. The information you subsequently develop as you pursue these "leads" will be almost wholly dependent upon your ingenuity and resourcefulness as an inspector.

Compliance Critieria for Records

Records are defined in 9 CFR 116.1 as "detailed records of information necessary to give a complete accounting of the activities within each establishment". The records will contain sufficient detail so that any person familiar with the production of the product can clearly understand each step in production.

Check on chronology. There should be no evidence entries are being recorded at any other time than at the time essential steps of production, testing, and destruction are actually being done. The steps should follow the same sequence that has been approved in an Outline of Production.

Check on identity of items. Records should sufficiently identify ingredients, cell passages, seed cultures, etc. so entries reflect precisely what is processed.

Check on dates. Records show the time and date(s) applicable to each step required. Be sure records are dated. Be sure time is recorded when essential to accurately assess the process as filed in The Outline of Production.

Check on quantity. Identity and quantity of ingredients, material, or product added or removed at each important step must be shown. Unusual gain or loss from start to finish must be accounted for.

Check on identity of personnel. Designated people shall initial or sign the records as they make measurements or judgments. These initials must be later identifiable.

Check on location of items. Locations of products in storage or in distribution shall be recorded so the items can be traced and located.

Check on legibility and indelibility of records. All records must be legible and indelible and kept for at least 2 years after the expiration date of the product. Records common to two or more lots of product should be traceable. All records must be available upon request.

Check for deviations from approved methods. Any deviations must be explained in enough detail to allow VS inspectors to judge whether purity, safety, efficacy, or potency of the product was affected. If products were judged to be adversely affected, a record from VS permitting the deviation must also be on file.

Two things must be stressed in record review:

1. Accountability
2. Identity

Use of Outlines of Production

The inspectors complete their review of the products that were tentatively selected and of worksheets prepared during the preinspection review.

Request the officially stamped copy of the Product Outline or special outline for the product, procedure, or equipment selected for examination.

Check the page dates against the preinspection notes.

Request completed detailed licensee records for the serial lot or other procedure selected.

Review the records and compare with requirements in the outline.

Observe procedures and compare with requirements in the outline.

Make notes on the product check-off sheets. Record all exceptions.

Check supporting records to substantiate the validity of the primary records.

Routines in Observation of Production Procedures

The inspector will schedule observations of production procedures from the production schedule provided by the firm and from preinspection notes.

Consult preinspection notes to assist in selecting critical procedures to observe and make actual selection.

Consign observation to one or more team members taking into consideration their field of specialization.

Check with the firm for production schedules, schedule changes and request to observe procedures.

Determine and follow specific restrictions necessary to enter limited access areas.

Take the assigned product and physically follow the route of movement from room to room within the facility. Compare with the blueprint check-off sheet; note if each activity is where preinspection notes indicate.

Spend enough time at each phase you are observing to thoroughly understand exactly what movements are being made in what sequence. Be able to do the complete sequence movements in your mind. Return to the outline and recheck correct procedure. Record any deviations.

Maintain an awareness of potential contamination, be aware of people's personal habits, environment factors affecting sterility, air movement, proximity to other organisms in use, etc.

Watch if routines for strict sterility are being broken, particularly harvest, bulk mixing, and fill.

Watch for deviations in proper lab procedure. - as placement of a sterile item on a non-sterile surface then reusing.

Observe if all surfaces of sterile rooms are being cleaned, walls and ceilings, as well as floors and lab tops.

Notice if the line supervisor is aware of the conditions or restrictions of the outline. Often outlines are written and filed by management without line supervisor involvement.

Watch measurement of ingredients - compare with allowed amounts in the outline.

Watch the recording of each step as it is done, verifying it is concurrent with operations.

Watch for evidence of reprocessing - watch steps taken post-incubation-compare with that allowed in outline. Keep sufficient notes on the observations to enable you to prove whether or not a procedure is according to the outline.

Call other inspectors to witness alleged exceptions. If procedure is dangerous to product or production people, call the team conference and request immediate review by firm personnel. TAKE ACTION.

Go into coolers, check if unlabeled serials can be mixed up. Check if unreleased serials can be mistakenly sold or distributed.

Recognize anything that is unlabeled or unidentified and require it be immediately identified and properly labeled, otherwise quarantine it and destroy under VS supervision.

Be on the lookout for organisms in abnormal amounts or in abnormal places as signs of possible research or extra testing in production areas - maintain an awareness of what organisms are authorized where.

Watch for activity in rooms where not so indicated in legends or blueprints.

Watch if proper lab clothing and if safety equipment is in use or only tokenly present.

Watch for movement of people through a restricted area who are on official business but are not observing the restrictions (maintenance men, firm executives).

Watch for nuisance things - food in coolers, lunching in lab rooms, desks and files in sterile rooms, lounging of idle employees in sterile rooms, (often these are hidden and make good places to avoid the supervisor).

Make notes on product check-off sheet. Record all exceptions and failure to follow good manufacturing practices.

Inspection of Controlled Equipment

The inspector checks the operating condition and regulation compliance of all automatically controlled equipment.

Review team assignments for observing firm's equipment. Be sure VS standard thermometers are available.

Review your preinspection list of firm's equipment. Add any new equipment found at the firm.

Observe working schedules and determine periods of high and low equipment use. Areas with constant temperature control should be checked during both the high and low activity periods and on several different days.

Schedule observation time with appropriate firm supervisory person. Determine and follow special procedures for entering limited access areas.

Place VS standardized thermometers in areas where temperature control is required and allow them to stabilize (about 5 minutes).

Determine if the temperature varies significantly from place to place in the enclosure.

Record at least three temperature readings on each piece of equipment where diverse activity periods could cause variation. Record time, location of the thermometer, and the identification of the equipment.

Record and compare the temperature being registered by the firm's equipment at the same time the VS reading is taken.

Compare VS thermometers with any thermometer encountered in use by the firm. Record location and concurrent readings of both.

Observe controlled freezing of completed product and note the time elapsing from harvest to reaching the final storage temperature. Compare freezing rate and time elapsed of outline requirements.

Observe sterilizers for loading that provides for circulation of heat or steam. If in doubt, place thermometer in center of load inside wrapped material.

Observe pasteurizers for temperature of both serum and water bath. Phenol or equivalent perservative must be provided to disinfect the VS thermometer before insertion into the heated serum. Air under pressure must be available to check the submerged can for leaks. The firm should be checking their pasteurizing recording equipment against accurate thermometers once a week or once every run if operated less often.

Observe lyophilizer and determine if each vial in the serial or subserial is being held and lyophilized under essentially identical conditions. Watch for shelf temperature variations, non-uniform stoppering, mixed container sizes in a unit, a subserial in more than one drying chamber, etc. If VS has granted permission to use multiple chambers for lyophilizing a subserial, determine if the conditions are uniform between chambers. If breakdowns have occurred, how are the vials handled. What do the records show. What precautions are taken.

Observe fermentors and determine if the environment provided the product is in accord with that specified in the outline. Review records and note breakdowns, manual operation, sterilization, automatic additions, maintenance of sterility.

Determine if the automatic controlling equipment is providing the environment within limits required by the outline or regulations. Note time, temperature, and recovery time after doors are opened, hot or cold material added, etc.

Determine how often the firm checks their equipment manually or with standardized measures.

Review the record keeping system. Be sure manual or standardizing checks are recorded.

Make notes on all equipment checked and record all exceptions to outline or regulation requirements.

DAILY TEAM REVIEW

The team leader daily assembles all members of the team.

Daily Team Review

Meet at a location where privacy is assured. This permits free discussion and prevents disclosures of privileged information.

Review the activities of each member of the team.

Discuss each exception found.

Tentatively rate each exception as minor, less serious, or serious.

Check the documentation of each exception to be sure it can be substantiated. Have it ready for the wrap-up session.

Discuss the next day's activities and modify assignments if indicated.

Prepare a summary of your findings and assemble a rough form of the inspection report as the inspection is winding up. Present your findings logically. Usually use the general inspection category outline in presenting exceptions. Cite 9 CFR references. Note where dates must be set for corrections or where supervisors must be told of significant items. Have the rough form ready for verbal presentation at the plant wrap-up session.

THE WRAP-UP SESSION

Identification of an exception is only a beginning. Compliance with regulations is the desired end result. Many exceptions can be satisfactorily handled through meeting with representatives of management at the conclusion of the inspection.

Preparation

Set the date for the wrap-up meeting with the official-in-charge as soon as you know when you will complete the inspection.

Encourage the official-in-charge to invite plant supervisory personnel to attend. You may wish to request that specific representatives attend so they may participate in discussions.

The wrap-up meeting usually concludes the in-plant portion of the inspection. The team leader leads the discussions between the team and the representatives of the licensee.

Presentation

Record the names of persons attending the wrap-up session.

Use the summary of exceptions prepared at the last team review session as the format for the verbal presentation.

Allow each team member who worked on the category in which the exception was found to present the findings and exception(s) he has found. The team leader maintains responsibility for developing all actions to be taken as a result of the discussion on each category.

Encourage an exchange of opinions with the representatives of the firm. Be sure any misconceptions or misunderstandings are resolved.

Record the important points that are brought out in the discussion. If some differences cannot be reconciled, tell the firm representatives that final actions will be determined after consultations with appropriate VS personnel.

Ask the firm representatives to suggest a date by which each exception will be corrected. If a date is not reasonable, try to set one by negotiation. If these approaches fail, assign a date by which corrections must be made.

Attempt to have written confirmation of all agreements made at the meeting returned to the licensee within 10 days of the conclusion of the inspection.

Keep three things in mind during all negotiations, discussions, and actions:

1. Is the action consistent with regulations?
2. Is the action consistent with VS policy?
3. Is the action reasonable?

Discourage tape recording the sessions. Taping tends to inhibit open and candid discussion. If a firm's secretary transcribes all or portions of the preceedings, insist that a copy be sent to the team leader.

Make favorable as well as unfavorable comments.

GUIDELINES FOR ACTIONS IN SPECIAL CIRCUMSTANCES

Inspectors will discover things which seem to indicate serious violations or willful non-compliance.

Document suspected or proven major violations using photostats of records, employee statements, and such other information as will stand legal scrutiny. See the section on Investigation of Alleged Violations in this manual for more information.

Impose a stop sale or hold release on products involved in a major violation. Do this only after exploring all aspects of the situation. DO NOT use this option too quickly.

Do not rescind a stop sale or hold release until the alleged violation is disproved or the need for it is clearly removed by subsequent events or instructions.

Maintain security on evidence of willful violations so the results of the investigation will not be compromised. Discuss evidence only with those who need to know.

TEAM WIND-UP MEETING

The team leader may again assemble the team at the inspection site after the wrap-up session to discuss tentative recommendations to be made, to plan for the writing of the inspection report, and to critique the inspection while still at the site.

Figure 4-1

PREINSPECTION

ESTABLISHMENT NOTES

PAGE: 1 OF 6
DATE: 9/19/7X
INSPECTOR: E. Ewell

FIRM: XYZ LABORATORIES

ESTABLISHMENT NUMBER: 999A
DATE ISSUED: 7-8-7X

OFFICIAL ADDRESS: 2100 Edgemoor
Wichita, Kan. 67208

MAILING ADDRESS: P.O. Box 762
Wichita, Kan 67208

SUBSIDIARIES OR DIVISIONS:
Sub Q Products, Inc.
XYZ International, Ltd
Div ABC Biologics, Inc.
MOM Industries, Inc

FIRM PHONE NO.: (409) 337-4692
CLOSEST FTS SWITCHBOARD CITY: Kansas City
COMMERCIAL FTS SWITCHBOARD NO.: (417) 339-0001

LOCATIONS OF LICENSED PREMISES:
2100 Edgemoor Ave, Wichita
425 West Street, Wichita
XYZ Ranch - RR#1 - Smith County, Duncan, Kan

OFFICIAL CONTACTS:
Dr Mark Sanborn - Lab Director
Dr James Nodding - Control Dept.

TYPE OF INSPECTION: In depth

SPECIAL REQUESTS FROM STAFF, LABORATORY, OTHERS:
1. Peters - Chem Lab, VSL
Check methods of formalin determination
2. Thompson - Licensing Staff
Recently applied to start Rabies Research
Examine facility for adequacy

ASSEMBLE AND ATTACH PERSONNEL LIST, PRODUCT LIST, BLUEPRINT NOTES, PRODUCT CHECK-OFF SHEETS AND OTHER PREINSPECTION NOTES AND WORKSHEETS.

PREINSPECTION

Figure 4-2

FIRM: XYZ Labs

PREINSPECTION WORKSHEET

EST. NO.: 999A PAGE: 2 OF 6

DATE: 9/19/7X INSPECTOR: EE

ADDITIONAL INFORMATION:

1. Previous Inspections:

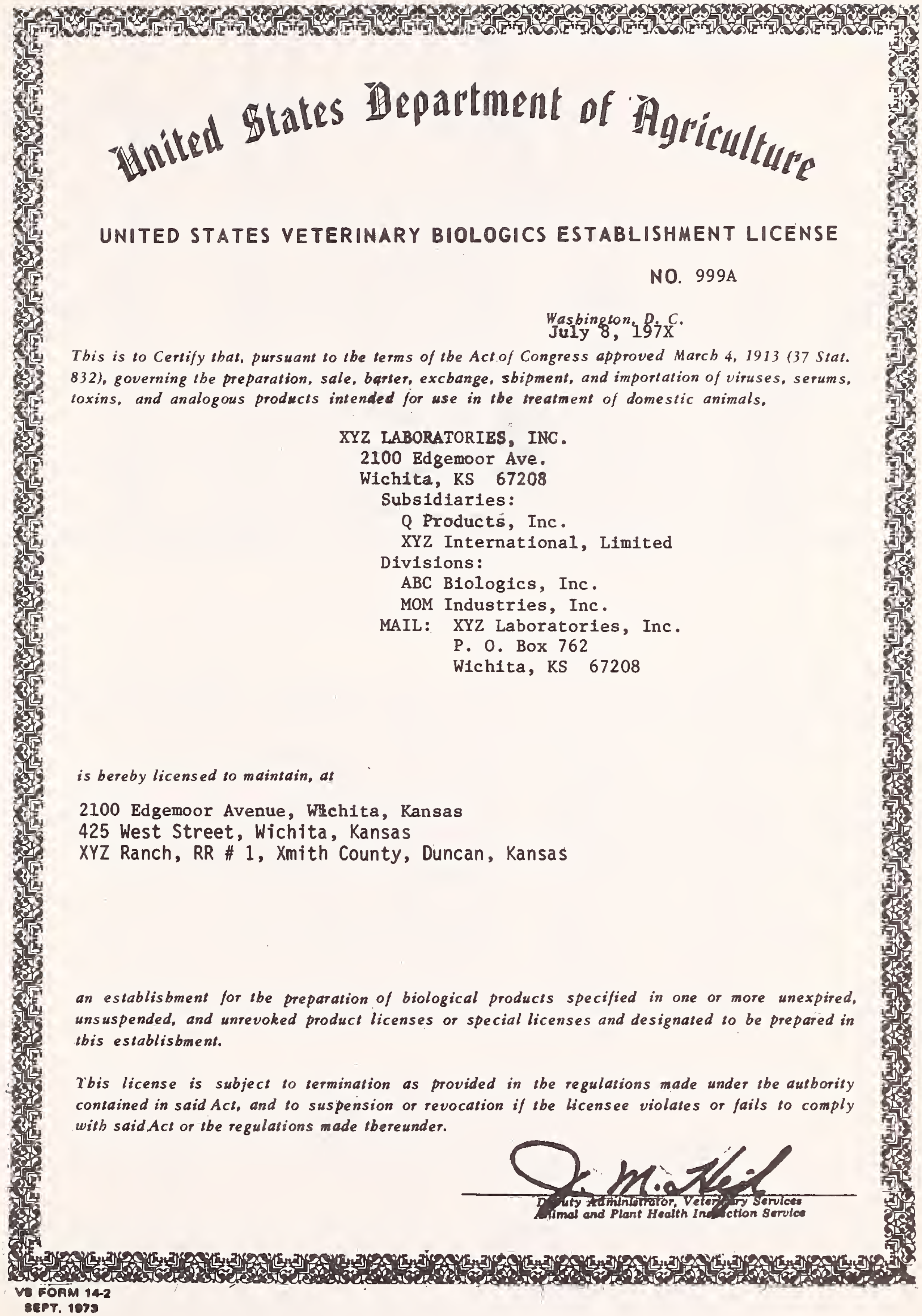
10/71	Spec.	Smith	4 Exceptions - Minor Sanitation
8/72	In Depth	Jones	6 Exceptions - One Less Serious Facilities Rest all minor Sani
5/73	In Depth	Smith	10 minor Sanitation items
6/73	Follow Up	Smith	Still not in Compliance Less Serious
7/73	Follow Up	Smith	Compliance acheived
3/74	Spec.	Jones	No exceptions

2. Unable to locate labels for Code 5021.00 Check firms file - Request new submissions

3. Having problems with drainage last inspection Be sure to check building 27

4. Unusual number of Consumer Complaints for CD-ICH. Check firms files

Figure 4-3



United States Department of Agriculture

UNITED STATES VETERINARY BIOLOGICS ESTABLISHMENT LICENSE

NO. 999A

Washington, D. C.
July 8, 197X

This is to Certify that, pursuant to the terms of the Act of Congress approved March 4, 1913 (37 Stat. 832), governing the preparation, sale, barter, exchange, shipment, and importation of viruses, serums, toxins, and analogous products intended for use in the treatment of domestic animals,

XYZ LABORATORIES, INC.
2100 Edgemoor Ave.
Wichita, KS 67208
Subsidiaries:
Q Products, Inc.
XYZ International, Limited
Divisions:
ABC Biologics, Inc.
MOM Industries, Inc.
MAIL: XYZ Laboratories, Inc.
P. O. Box 762
Wichita, KS 67208

is hereby licensed to maintain, at

2100 Edgemoor Avenue, Wichita, Kansas
425 West Street, Wichita, Kansas
XYZ Ranch, RR # 1, Xmith County, Duncan, Kansas

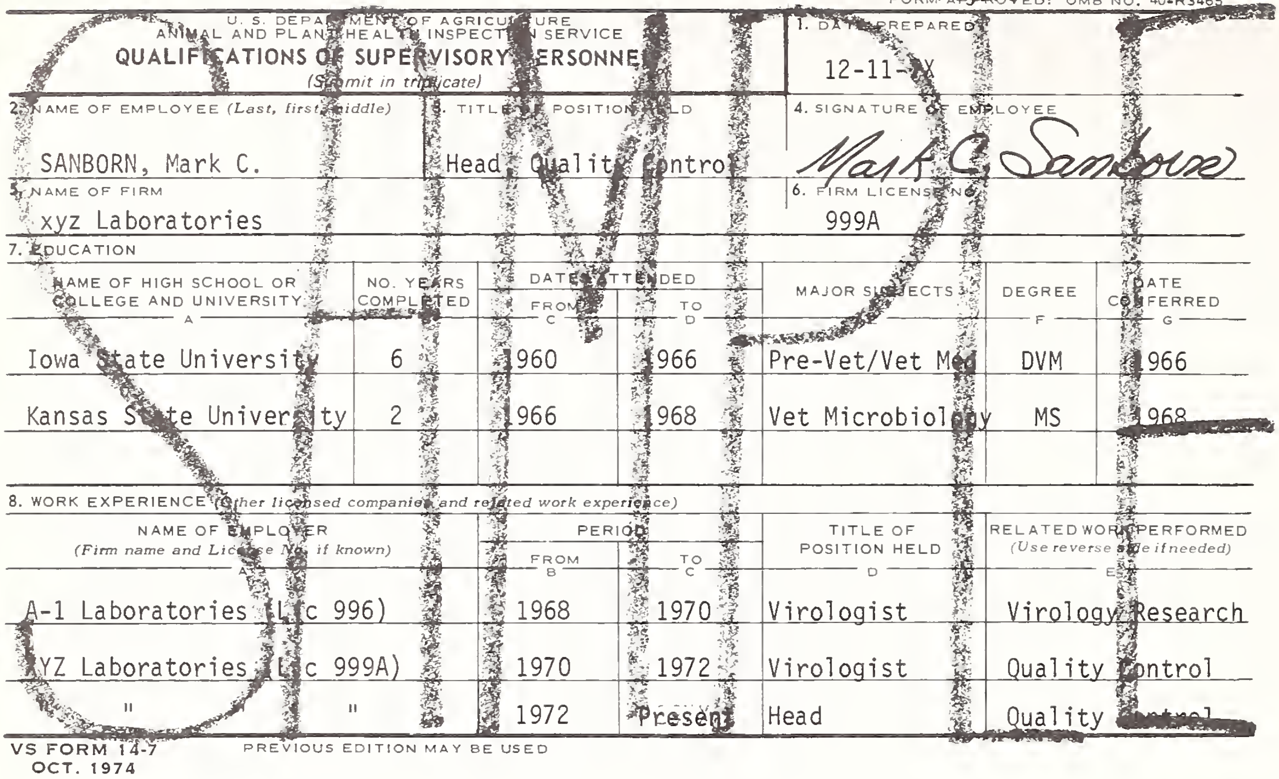
an establishment for the preparation of biological products specified in one or more unexpired, unsuspended, and unrevoked product licenses or special licenses and designated to be prepared in this establishment.

This license is subject to termination as provided in the regulations made under the authority contained in said Act, and to suspension or revocation if the licensee violates or fails to comply with said Act or the regulations made thereunder.

Deputy Administrator, Veterinary Services
Animal and Plant Health Inspection Service

VS FORM 14-2
SEPT. 1973

Figure 4-4



FORM APPROVED: OMB NO. 40-R3465

U. S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
QUALIFICATIONS OF SUPERVISORY PERSONNEL
(Submit in triplicate)

SAMPLE

1. DATE PREPARED: 12-11-7X

2. NAME OF EMPLOYEE *(Last, first, middle)*: SANBORN, Mark C.

3. TITLE OF POSITION HELD: Head, Quality Control

4. SIGNATURE OF EMPLOYEE: Mark C. Sanborn

5. NAME OF FIRM: xyz Laboratories

6. FIRM LICENSE NO.: 999A

7. EDUCATION

NAME OF HIGH SCHOOL OR COLLEGE AND UNIVERSITY A	NO. YEARS COMPLETED	DATES ATTENDED FROM C	DATES ATTENDED TO D	MAJOR SUBJECTS	DEGREE F	DATE CONFERRED G
Iowa State University	6	1960	1966	Pre-Vet/Vet Med	DVM	1966
Kansas State University	2	1966	1968	Vet Microbiology	MS	1968

8. WORK EXPERIENCE *(Other licensed companies and related work experience)*

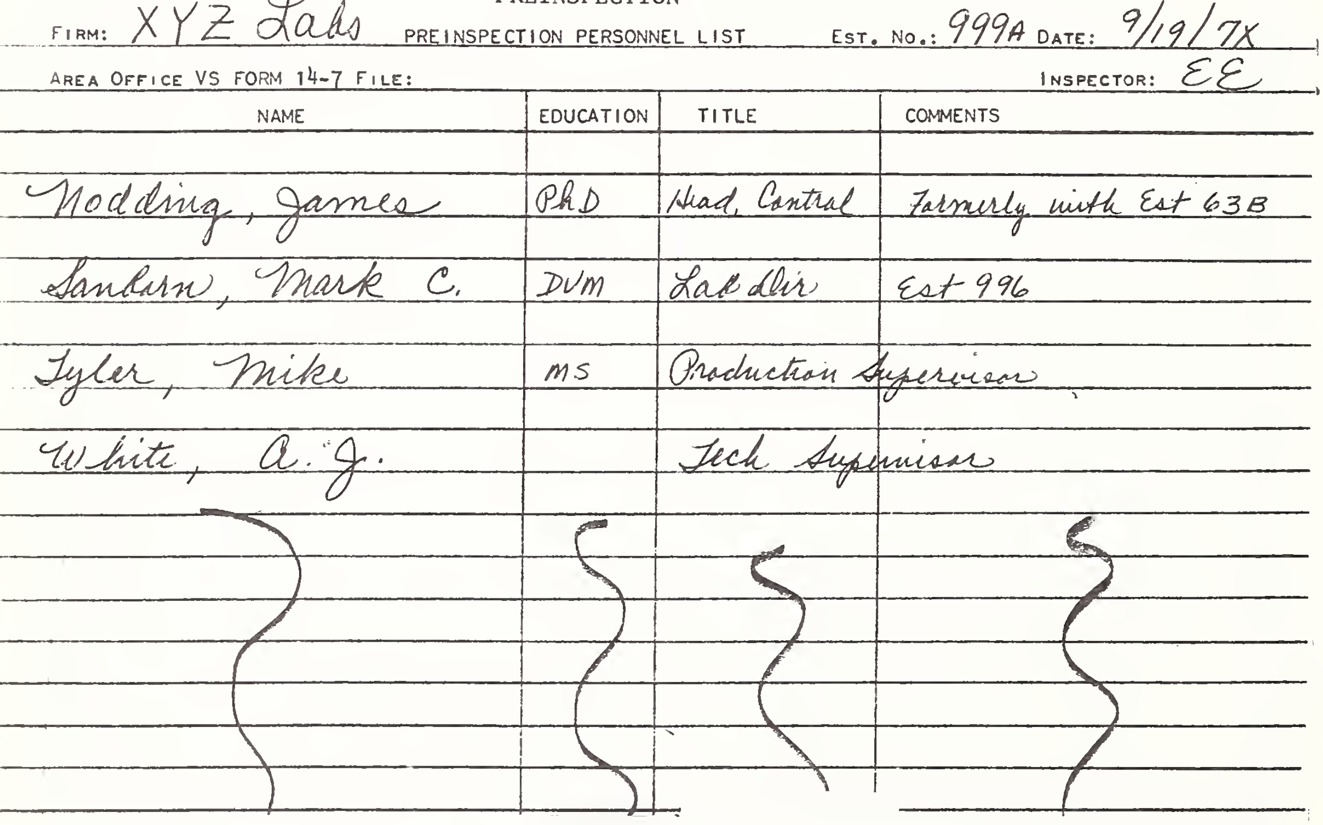
NAME OF EMPLOYER *(Firm name and License No. if known)* A	PERIOD FROM B	PERIOD TO C	TITLE OF POSITION HELD D	RELATED WORK PERFORMED *(Use reverse side if needed)* E
A-1 Laboratories (Lic 996)	1968	1970	Virologist	Virology Research
XYZ Laboratories (Lic 999A)	1970	1972	Virologist	Quality Control
" "	1972	Present	Head	Quality Control

VS FORM 14-7
OCT. 1974

PREVIOUS EDITION MAY BE USED

Figure 4-5

PREINSPECTION



FIRM: XYZ Labs

PREINSPECTION PERSONNEL LIST

EST. NO.: 999A DATE: 9/19/7X

AREA OFFICE VS FORM 14-7 FILE:

INSPECTOR: EE

NAME	EDUCATION	TITLE	COMMENTS
Nodding, James	PhD	Head, Control	Formerly with Est 63B
Sanborn, Mark C.	DVM	Lab dir	Est 996
Tyler, Mike	MS	Production Supervisor	
White, A. J.		Tech Supervisor	

Figure 4-6

LICENSE 999A XYZ LABORATORY DATE - 07/07/76

VACCINES AND VIRUSES

Preinspection Status
9/10/76 DCR

ISSUE DATE	PRODUCT	TRUE NAME
05/09/75	1101.00	BOVINE RHINOTRACHEITIS V, MLV, TCO - Inactive - Last serial harvested 7/4/74
05/09/75	1119.00	BOVINE RHINOTRACHEITIS V-LEPTO POMONA BACTERIN,MLV,TCO,COMB PKG
05/09/75	1121.00	BOVINE RHINOTRACHEITIS-PI3 V, MLV, TCO - Active
02/19/75	1149.00	BOVINE RHINOTRACHEITIS-PI3 V- PAST HEMO-MULTO BACT,MLV,TCO, COMB PKG
05/09/75	1171.00	BOVINE RHINOTRACHEITIS-VIRUS DIARRHEA-PI3 V, MLV, TCO Active
02/19/75	1199.00	BOV RHINO-VIRUS DIARRHEA-PI3 V-PAST HEMO-MULTO BACT,MLV,TCO, COMB PKG
05/09/74	1201.00	BOVINE VIRUS DIARRHEA V, MLV, TCO - Inactive - Last serial harvested 4/9/71 - over 5 years
05/09/75	1301.20	CANINE DISTEMPER V, MLV, CLO - only 3-4 serials per year
05/09/75	1311.20	CANINE DISTEMPER-HEPATITIS V, MLV, CLO - 40 serials per year
05/09/75	1329.20	CANINE DISTEMPER-HEPATITIS V- LEPTO BACT,MLV,CLO,COMB PKG
11/11/74	1381.20	CANINE DISTEMPER-HEPATITIS- PI V,MLV,CLO - Big # - 85 serials a year
12/12/74	1399.20	CANINE DISTEMPER-HEPATITIS- PI V-LEPTO BACT,MLV,CLO, COMB PKG
11/18/75	1421.20	CANINE PARAINFLUENZA V, MLV, CLO - new product Lic 6/10/76
05/09/75	1565.00	FELINE PANLEUKOPENIA VACCINE, KV, TCO - Seasonal Production 2-3 serials/year
04/16/76	1611.20	FELINE RHINOTRACHEITIS V, MLV, CLO - 10 serials per year
03/20/75	1629.30	FELINE RHINOTRACHEITIS- PANLEUKOPENIA V,MLV,CLO&,TCO, COMB PKG
09/16/75	1631.20	FELINE RHINOTRACHEITIS-CALICI V,MLV,CLO - 5 serials per year
09/16/75	1649.30	FELINE RHINOTRACHEITIS-CALICI- PANLEUKOPENIA V,MLV&,KV,CLO&,TCO, COMB PKG

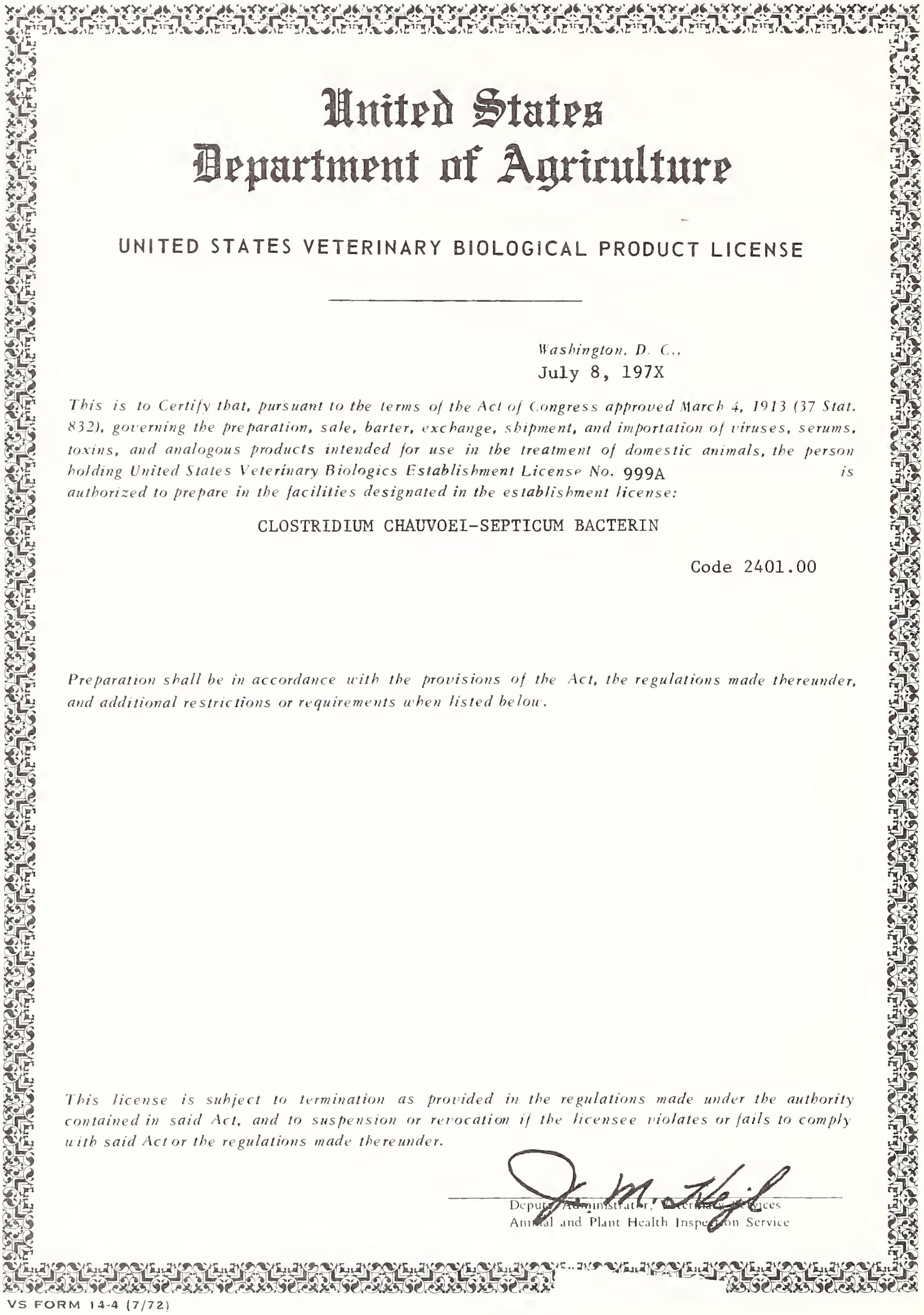
BACTERINS

ISSUE DATE	PRODUCT	TRUE NAME
05/09/75	2641.20	ERYSIPELOTHRIX RHUSIOPATHIAE BACTERIN, 2CC DOSE - 15 serials per year
05/09/75	2671.00	LEPTOSPIRA CANICOLA- ICTEROHAEMORRHAGIAE BACTERIN - 40 serials/year
05/09/75	2691.20	LEPTOSPIRA POMONA BACTERIN, 2CC DOSE - 15 serials per year
02/05/75	2700.00	PASTEURELLA HAEMOLYTICA-MULTO BACTERIN, BOVINE ISOLATES - 20 serials/year

DIAGNOSTICS

ISSUE DATE	PRODUCT	TRUE NAME
02/05/74	5021.00	CANINE BRUCELLOSIS AGGLUTINATION ANT & REAGENT SERUM,CO - 2-3 per year - special orders
07/03/74	5515.20	EQUINE INFECTIOUS ANEMIA IMM ANT & REAGENT SERUM,CLO,EO - 10 serials per year

Figure 4-7



United States Department of Agriculture

UNITED STATES VETERINARY BIOLOGICAL PRODUCT LICENSE

Washington, D. C.,
July 8, 197X

This is to Certify that, pursuant to the terms of the Act of Congress approved March 4, 1913 (37 Stat. 832), governing the preparation, sale, barter, exchange, shipment, and importation of viruses, serums, toxins, and analogous products intended for use in the treatment of domestic animals, the person holding United States Veterinary Biologics Establishment License No. 999A *is authorized to prepare in the facilities designated in the establishment license:*

CLOSTRIDIUM CHAUVOEI-SEPTICUM BACTERIN

Code 2401.00

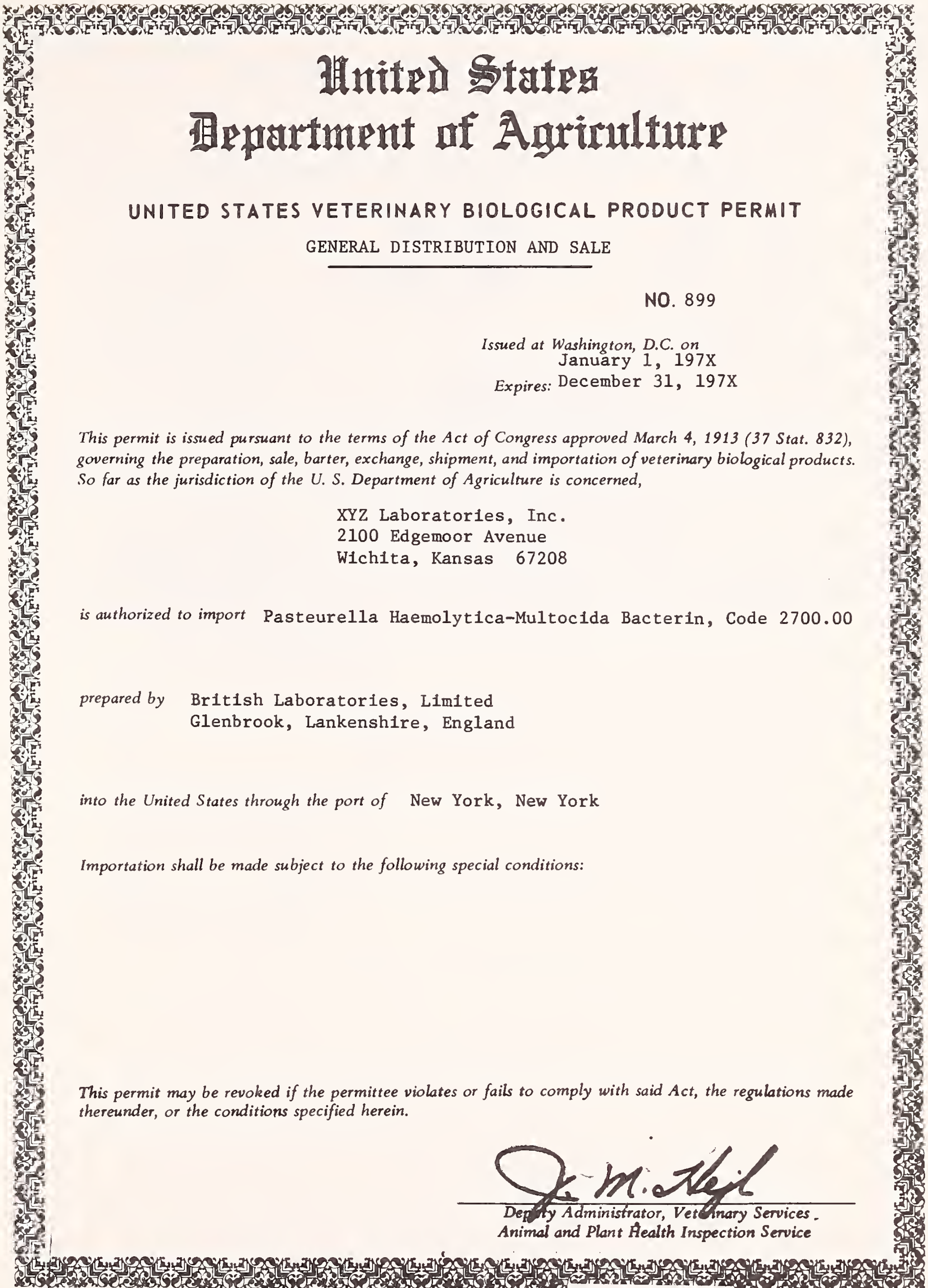
Preparation shall be in accordance with the provisions of the Act, the regulations made thereunder, and additional restrictions or requirements when listed below.

This license is subject to termination as provided in the regulations made under the authority contained in said Act, and to suspension or revocation if the licensee violates or fails to comply with said Act or the regulations made thereunder.

Deputy Administrator, Veterinary Services
Animal and Plant Health Inspection Service

VS FORM 14-4 (7/72)

Figure 4-8



United States Department of Agriculture

UNITED STATES VETERINARY BIOLOGICAL PRODUCT PERMIT

GENERAL DISTRIBUTION AND SALE

NO. 899

Issued at Washington, D.C. on January 1, 197X
Expires: December 31, 197X

This permit is issued pursuant to the terms of the Act of Congress approved March 4, 1913 (37 Stat. 832), governing the preparation, sale, barter, exchange, shipment, and importation of veterinary biological products. So far as the jurisdiction of the U. S. Department of Agriculture is concerned,

XYZ Laboratories, Inc.
2100 Edgemoor Avenue
Wichita, Kansas 67208

is authorized to import Pasteurella Haemolytica-Multocida Bacterin, Code 2700.00

prepared by British Laboratories, Limited
Glenbrook, Lankenshire, England

into the United States through the port of New York, New York

Importation shall be made subject to the following special conditions:

This permit may be revoked if the permittee violates or fails to comply with said Act, the regulations made thereunder, or the conditions specified herein.

Deputy Administrator, Veterinary Services
Animal and Plant Health Inspection Service

VS FORM 14-6
MAR. 1974

Figure 4-9

PREINSPECTION
PRODUCT CHECK-OFF SHEET

PRODUCT CODE: 2401.00

EST. NO.: 999A DATE: 9/20/7X

NAME: Clostridium Chauvoei-Septicum Bacterin INSPECTOR: EE

TRADE NAME: Clo Cha - Sept Bacterin

DATE PRODUCT LICENSE ISSUED: 7-8-7X

OUTLINE STAMP DATE: 4-3-7X PAGE REVISION DATES: p 4,5,6 5/10/7X p 20 6/1/7X

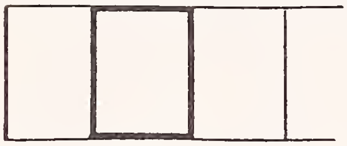
LABELED FOR:	MOM	Q Prod	XYZ Labs
SIZE:	100 250	250 500	50 150
CONTAINER NO.:	#425 #426	#447 #462	#560 #561
CARTON NO.:	#427 #428	#448 #463	#562 #563
ENCLOSURE NO.:	#430	#449	#564

GENERAL NOTES FROM THE OUTLINE:	SUGGESTED SERIALS TO REVIEW
EXPIRATION DATING: 36 mo. from Harvest	#493
DOSAGE: 10 ml twice Bovine	#679
APPROVED SIZES: 50, 100, 150, 250, 500	#972 - DBF - Potency
FILL INFO: 50-53, 100-103, 150-153, 250-255, 500-505	#973 - NR Potency
	#975
TESTING RECORD:	ANNUAL PRODUCTION
Potency Problem Serials 972 & 73	25 serials in 197X
all others sat	

Figure 4-10

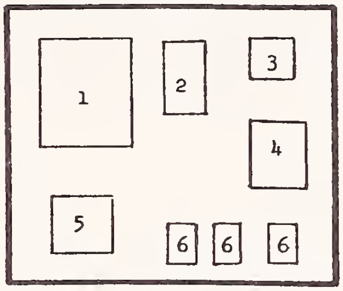
EXAMPLES OF PLOT PLANS

1. Entire building being plot plan.



Boundary line.

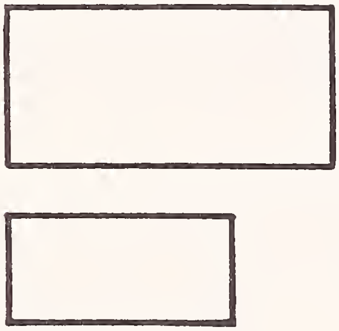
2. Many buildings on same plot plan or premises.



1. Production of Vet. Biologics; blueprint required.
2. Separate research facility; blueprint not required.
3. Human biologics production; blueprint not required.
4. Pharmaceutics building; blueprint not required.
5. Shipping facility, including Vet. Biol.; blueprint required.
6. Testing facility for Vet. Biol.; blueprint required.

Boundary line.

3. Same establishment on separate premises. Separate plot plans and blueprints required.



Boundary line.

A = AIR
G = GAS
H = HOT WATER
C = COLD WATER
▨ = DRAIN

ADEQUATE LIGHTING IS PROVIDED

5	VACUUM PUMP #1
6	REVCO FREEZER
7	CENTRIFUGE #1
8	FREEZER #2
9	VACUUM PUMP #2
10	VACUUM PUMP #3
11	LIQUID NITROGEN TANK
12	INCUBATOR
12-A	FREEZER #1
13	CENTRIFUGE #2
14	REFRIGERATOR #1
15	MICROSCOPE #1
16	MICROSCOPE #2
17	LIQUID NITROGEN TANK
18	JAMESWAY EGG INCUBATOR

Figure 4-11

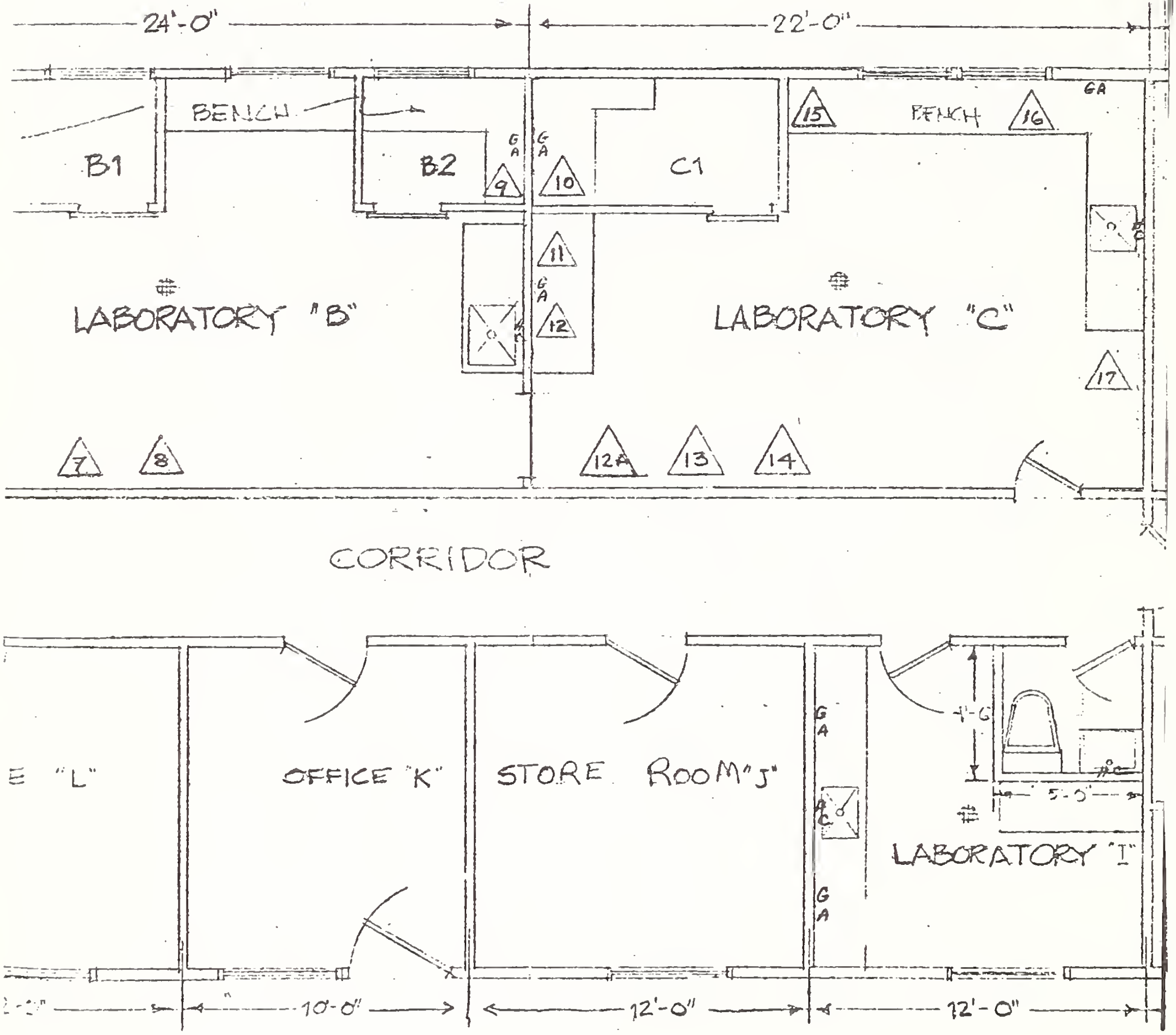


Figure 4-12

PREINSPECTION

PREINSPECTION BLUEPRINT WORKSHEET

FIRM: XYZ Labs

EST. NO.: 999A PAGE: 1 OF 2

DOCUMENT IDENTIFICATION:

DATE: 9/21/7X INSPECTOR: EE

BUILDING OR PLOT	STAMP DATE	LEGEND PAGE	STAMP DATE
2100 Edgemon Plot	9/10/65	p 1-6	9/10/65
		p 7-9	4/3/72
Bldg 10	9/10/65	p 1-20	9/10/65
Bldg 12	9/10/65	p 1-12	4/3/72
Bldg 14	7/6/69	p 1,3,7-10	7/6/69
		p 2,4-6	10/14/69
425 West St. Plot	4/16/74	p 1-4	4/16/74
Bldg 20	4/16/74	p 1,7-15	4/16/74
		p 2-6	4/25/75
XYZ Ranch Plot (Includes Bldg print)	9/10/65	p 1-3	9/10/65

ADDITIONAL FACILITY INFORMATION:
(SEE ATTACHED CHECK LIST)

1. Check Bldg 27 at Ranch for drainage problems
2. Bldg 10 proposed for Rabies production

Figure 4-13
BLUEPRINT

CHECKLIST

FOR

CODE

CODE	SEED & STOCK PREP & STOR	CELL PREP	MEDIA PREP	PROD CONTAINER PREP	INOCULATION	INCUBATION	HARVEST	INACTIVATION	CONCENTRATION	POOL & BULK	BULK STORAGE	FINAL CONTAINER PREP	FILLING	FREEZING	DESICCATION	FINAL PRERELEASE STORAGE	LABELLING	PACKAGING	RELEASED STORAGE & SHIPPING	PURITY TESTS	SAFETY TESTS	POTENCY TESTS	MOISTURE & PRESERVATIVE TESTS	checked by (initials)	date checked
IBR	10A	10Z	10F	14	10^{D}	10^{E}	10^{D}	~~10~~	[illegible]	10^{K}	10^{R}	14	14	10^{A}	14	14	14	14	14	20	20	20	20	EE	9/23
BVD	10B	10Z	10F	14	10^{B}	10^{E}	10^{B}	—	—	10^{K}	10^{R}	14	14	10^{A}	14										
CD	10C	10Z	10F	14	10^{C}	10^{E}	10^{C}	—	—	10^{K}	10^{R}	14	14	10^{A}	14										
ICH	12F	10Z	12D	14	12^{F}	12^{R} ~~10~~	12^{F}	—	—	10^{K}	10^{R}	14	14	10^{A}	14							✓			
CHAUV. # X2	20A	-	20K	14	20^{A}	20^{R}	20^{C}	20^{R}	20^{C}	20^{C}	20^{T}	14	14	—	-							Rand			
CHAUV # X14	20A	-	20K	14	20^{A}	20^{R}	20^{C}	20^{R}	20^{C}	20^{C}	20^{T}	14	14	—	—										
SEPT # 23	20A	-	20K	14	20^{A}	20^{R}	20^{C}	20^{R}	20^{C}	20^{C}	20^{T}	14	14	—	—	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

```
                                    APHIS - VS      VETERINARY BIOLOGICS PROGRAM                              08/06/76
                  BIOLOGICS PRODUCTS PRODUCT AND TESTING SUMMARY FOR:  MARCH 1976
                                                  SUMMARY BY LICENSEE                                          PAGE  1

                     NO.   NO. PERCENT SERIALS NO. PERCENT ***** CORRELATION *****      TOTAL        TOTAL  OTHER OTHER
   LIC  PRODUCT SERIALS  UNSAT  FIRM  TESTED UNSAT  VB    EFR/  EFR/  DBF/  EXCEP      DOSES        DOSES TESTED UNSAT
   NO.   CODE  PRODUCED FIRM   UNSAT    VB    VB   UNSAT  NBT   SAT   NBT   TION     PRODUCED    DESTROYED   VB    VB

   997  1311.00      7     0    0.0     5     0    0.0     2     5     0     0      256,598            0     0     0

   997  1325.50      1     0    0.0     1     1  100.0     0     0     0     1       21,090       21,090     0     0
 * 997  1329.00     17     0    0.0     0     0    0.0    17     0     0     0      196,850            0     0     0
 * 997  1349.00      1     0    0.0     0     0    0.0     1     0     0     0        3,000            0     0     0

   997  1561.00      1     0    0.0     0     0    0.0     1     0     0     0       40,635            0     0     0
   997  1565.00      1     0    0.0     0     0    0.0     1     0     0     0       26,881            0     0     0
   997  1581.10      1     0    0.0     1     0    0.0     0     1     0     0       12,546            0     0     0

   997  1901.11     10     0    0.0     7     0    0.0     3     7     0     0      202,273            0     0     0
   997  2641.20      4     0    0.0     1     0    0.0     3     1     0     0      718,650            0     0     0
   997  2671.00      8     0    0.0     1     0    0.0     7     1     0     0      153,559            0     0     0

 TOTAL: 997         51     0    0.0    16     1    6.2    35    15     0     1    1,632,082       21,090     0     0
 MINUS COMB PKG     33     0    0.0    16     1    6.2    17    15     0     1    1,432,232       21,090     0     0


   998  1051.11      2     0    0.0     1     0    0.0     1     1     0     0    3,799,000            0     0     0
   998  1621.10      2     0    0.0     2     0    0.0     0     2     0     0   13,612,500            0     0     0
   998  1641.00      7     0    0.0     3     0    0.0     4     3     0     0   17,003,000            0     0     0

   998  1641.01      3     0    0.0     3     0    0.0     0     3     0     0    5,822,000            0     0     0
   998  1761.11      2     0    0.0     2     0    0.0     0     2     0     0   18,670,000            0     0     0
   998  1881.10      3     0    0.0     3     1   33.3     0     2     0     1   19,071,000    6,326,500     0     0

   998  5206.00      3     0    0.0     3     0    0.0     0     3     0     0      897,000            0     0     0

 TOTAL: 998         22     0    0.0    17     1    5.8     5    16     0     1   78,874,500    6,326,500     0     0


   999A 1101.00      3     0    0.0     2     0    0.0     1     2     0     0      454,440            0     0     0
   999A 1121.00      1     0    0.0     0     0    0.0     1     0     0     0       83,380            0     0     0
   999A 1151.00      3     0    0.0     1     0    0.0     2     1     0     0      441,060            0     0     0

   999A 1171.00      2     0    0.0     1     0    0.0     1     1     0     0      201,425            0     0     0
   999A 1201.00      1     0    0.0     0     0    0.0     1     0     0     0      112,750            0     0     0
   999A 1311.00      1     0    0.0     0     0    0.0     1     0     0     0       18,556            0     0     0

   999A 1561.00      1     0    0.0     1     0    0.0     0     1     0     0       25,497            0     0     0
   999A 1961.00      1     0    0.0     0     0    0.0     1     0     0     0       37,060            0     0     0
   999A 2401.00      1     0    0.0     1     0    0.0     0     1     0     0      267,500            0     0     0

   999A 2465.90      1     0    0.0     0     0    0.0     1     0     0     0       52,050            0     0     0
   999A 2641.20      3     0    0.0     2     0    0.0     1     2     0     0      341,775            0     0     0
   999A 2671.00      2     0    0.0     2     0    0.0     0     2     0     0      107,031            0     0     0

 * COMBINATION PACKAGE
END OF DATA
```

U. S. DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
VETERINARY BIOLOGICS DIVISION
FEDERAL CENTER BUILDING
HYATTSVILLE, MARYLAND 20782

TRANSMITTAL OF LABELS AND CIRCULARS OR OUTLINES

NOTE: Submit original and 6 copies. Retain last copy.

FORM APPROVED BUDGET BUREAU NO. 40R5[illegible]

1. NAME AND ADDRESS OF LICENSEE *(Include Zip Code)*

Figure 4-15

2. DATE OF PRIOR RELATED CORRESPONDENCE

3. ESTABLISHMENT LICENSE NO.

4. DATE SUBMITTED

5. NAME OF PRODUCT *(Use separate form for each product)*

6. PRODUCT CODE

7. CHECK IF NEW PRODUCT ☐

LABELS AND CIRCULARS SUBMITTED

TYPE	FINISHED			SKETCHES		
	NO. SETS A	NO. COPIES OF EACH B	ITEM ON FILE BEING REPLACED *(Give No. (s))* C	NO. SETS D	NO. COPIES OF EACH E	ITEM ON FILE BEING REPLACED *(Give No. (s))* F
8. CONTAINER						
9. BOX						
10. CIRCULARS						
11. OTHER						

OUTLINE SUBMITTED *(Do no submit with same form covering Labels and Circulars)*

12. NO. COPIES

13. TYPE OF SUBMISSION

NEW OUTLINE ☐ COMPLETE REVISION ☐ PAGES AMENDED ☐ PAGES ADDED ☐

14. PAGE NUMBERS AMENDED OR ADDED

15. DATE OF PREVIOUS OUTLINE

16. COMMENTS

17. SIGNATURE OF LICENSEE REPRESENTATIVE

18. TITLE

REVIEW BY VETERINARY BIOLOGICS DIVISION

19. EXCEPTIONS

Directive: BP Memo No. 7, for submission of outlines
Submitted by licensee

Directive: BP Memo No. 8, for submission of labels,
circulars and sketches by licensee

20. REVIEWED BY *(Signature, Veterinary Biologics Licensing)*

21. DATE RETURNED

VB FORM 15
AUG 1965

REPLACES AIQ FORM 84, WHICH IS OBSOLETE

Figure 4-16

U. S. DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
VETERINARY BIOLOGICS DIVISION

APPLICATION FOR
UNITED STATES VETERINARY BIOLOGICS ESTABLISHMENT LICENSE

FORM APPROVED:
BUDGET BUREAU NO. 40-R2715

FOR VS USE ONLY

ESTABLISHMENT LICENSE NO.

INSTRUCTIONS: Submit one copy of application for each establishment. If additional space is needed, attach additional sheets and refer to item No. Attach plot plans, blueprints, and supporting documents in triplicate.

1. TYPE OF APPLICATION *(Check one)*
INITIAL ☐ CHANGE OF LICENSE ☐

2. DATE SUBMITTED

3. NAME AND ADDRESS OF APPLICANT *(Include No., Street or RFD No., City, State, Zip Code)*

4. IF INITIAL APPLICATION, ATTACH A COMPLETED VB FORM 3 FOR ONE PRODUCT. NAME THE PRODUCT

5. IF CHANGE OF LICENSE, EXPLAIN PURPOSE OF CHANGE

6. TYPE OF ORGANIZATION *(Check one)*
CORPORATION ☐ PARTNERSHIP ☐ INDIVIDUAL PROPRIETORSHIP ☐

7. IF CORPORATION GIVE STATE IN WHICH INCORPORATED *(Attach certified copy of articles of incorporation)*

8. PRINCIPAL OFFICERS OR PARTNERS

NAME OF EACH A	TITLE B	BUSINESS ADDRESS *(No., Street or RFD No., City, State, Zip Code)* C

9. IDENTIFY EACH SUBSIDIARY TO OPERATE IN THE ESTABLISHMENT
(Attach a certified copy of articles of incorporation and a letter of approval signed by an authorized officer of each subsidiary named)

NAME AND LOCATION OF EACH SUBSIDIARY A	STATE IN WHICH INCORPORATED B

10. LIST THE LOCATION OF ALL PREMISES TO BE USED FOR PRODUCTION AND INITIAL SHIPPING *(If different from item 3)*

CERTIFICATION

In accordance with the Act of Congress approved March 4, 1913 (37 Stat. 832-833; 21 U. S. C. 151-158), application is hereby made for a license to maintain an establishment for the production of viruses, serums, toxins, or analogous products, for use in the treatment of domestic animals. If a license is issued by the United States Department of Agriculture under this application, the licensee expressly agrees to comply with the provisions of the said Act, and all rules, regulations, and orders of the Department issued pursuant thereto relating to the operation of such establishment and the preparation, testing, and distribution of biological products prepared therein, and that the said biological products will not be labeled or advertised so as to mislead or deceive the purchaser in any particular.

IF CORPORATION, APPLY SEAL HERE

11. SIGNATURE OF AUTHORIZED OFFICIAL

12. TITLE

13. DATE SIGNED

Figure 4-17

WBBS - APPROVED WORKLOAD AND WORK PERFORMED REPORT	5TH-ORDER WORK-UNIT 600 - VETERINARY BIOLOGICS ACTIVITY	STATE IOWA	MONTH AND YEAR NOVEMBER 1976

4TH-ORDER WORK-UNIT		FORECAST			WORK COUNTS		MAN-HOURS PRODUCED		
CODE A	TITLE B	REPORTING TIME VALUE C	TOTAL WORK UNITS D	TOTAL MAN-HOURS E	THIS PERIOD F	ACCUMULATIVE G	THIS PERIOD H	ACCUMULATIVE I	~~PERCENT ACCOMPLISHED (Col. I ÷ Col. E)~~ J
01	Biologics Samples Collected and Serials Destroyed	6.25	187	1170	16				ACTUAL HOURS
	Key: Enter Establishment								(NOT REQUIRED)
02	Biologics Product User Complaints	13.3	15	200	2				4
	Key: Complaint Received								
03	Indepth Establishment Inspections	479	5	2395	1				263
	Key: Enter Establishment								
04	Follow-Up Establishment Inspections	98	5	490	0				
	Key: Enter Establishment								
05	Special Establishment Inspections	83	5	415	2				72
	Key: Enter Establishment								
06	Alleged VST Act Violations Investigated	285	4	1140	2				61
	Key: Information Received - Number Assigned								
07	Program Co-ordination Activity - Report Actual	---	hours	2200			190		190
	Hours								
08	Program Training Activity - Report Actual Hours	---	hours	400			27		27
	TOTALS *(Col. E, H I, and J)*				▨	▨			

VS FORM 8-76
JULY 1976

PREVIOUS EDITIONS ARE OBSOLETE

USDA - APHIS

FIGURE 4-18

FORM APPROVED: OMB NO. 40-R3460

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES

1. DATE SUBMITTED 3-27-7X

2. FIRM LICENSE NO. 999A

3. NAME AND MAILING ADDRESS OF FIRM *(Include Zip Code)*

XYZ Laboratories
P.O. Box 762
Wichita, KS 67208

INSTRUCTIONS: Submit original and one copy with samples. **(Leave First Carbon Intact.)**

4. PURPOSE
ROUTINE CONCURRENT SAMPLE ☒ PRELICENSING SAMPLE ☐
RETENTION SAMPLE ☐ RESUBMISSION ☐ *(Specify in remarks)* OTHER ☐ *(Specify in remarks)*

5. HOW IS PRODUCT SHIPPED
DRY ICE ☐ WATER-ICED ☒ UNREFRIGERATED ☐

OTHER *(Specify)*

PRODUCT IS SHIPPED VIA United Parcel Service

PRODUCT NAME 6	PRODUCT CODE 7	SERIAL NO. 8	SAMPLE CODE *(For Gov't Use Only)* 9	HARVEST DATE 10	EXPIRATION DATE 11	SAMPLE CONTAINERS SUBMITTED NO. 12	SIZE 13	FIELD DOSE 14	INDICATE BULK OR FINAL 15
Clostridium Chauvoei Septicum Bacterin	2401.00	1313		3-1-7X	3-1-7Y	13	50D 250CC	5CC	Final
Autogenous Bacterin Lapine Isolates-Aqueous	2051.03	421		3-2-7X	9-2-7X	2	50CC in 250's		
Clostridium Chauvoei Septicum Bacterin	2401.00	** 1312		2-28-7X	2-28-7Y	20	50D 250CC	5CC	Final
Erysipelothrix Rhusiopathiae Bacterin	2461.20	258		2-23-7X	2-23-7W	2	50D 100CC	2CC	Bulk

16. REMARKS

** Per request of Dr. Freeman dated 3-25-7X
Resubmission

17. IF THIS FORM IS NOT USED TO AUTHENTICATE SAMPLES ATTACH COPIES OF ALTERNATE FORMS FOR ALL SERIALS LISTED ABOVE.

18. SIGNATURE OF FIRM REPRESENTATIVE

FOR OFFICIAL GOVERNMENT SAMPLER

19. NUMBER OF SERIALS SAMPLED AND LISTED ON THIS PAGE 2

20. REMARKS Serial 421 and 258 not authenticated. Other samples packaged, sealed with tape and initialed (RM), dated 3-27-7X

21. SIGNATURE Ralph Maloney

22. TITLE Animal Health Tech

23. DATE 3-27-7X

ACKNOWLEDGEMENT OF RECEIPT OF SAMPLES

24. CONDITION AND REMARKS

25. RECEIVED BY *(Signature)*

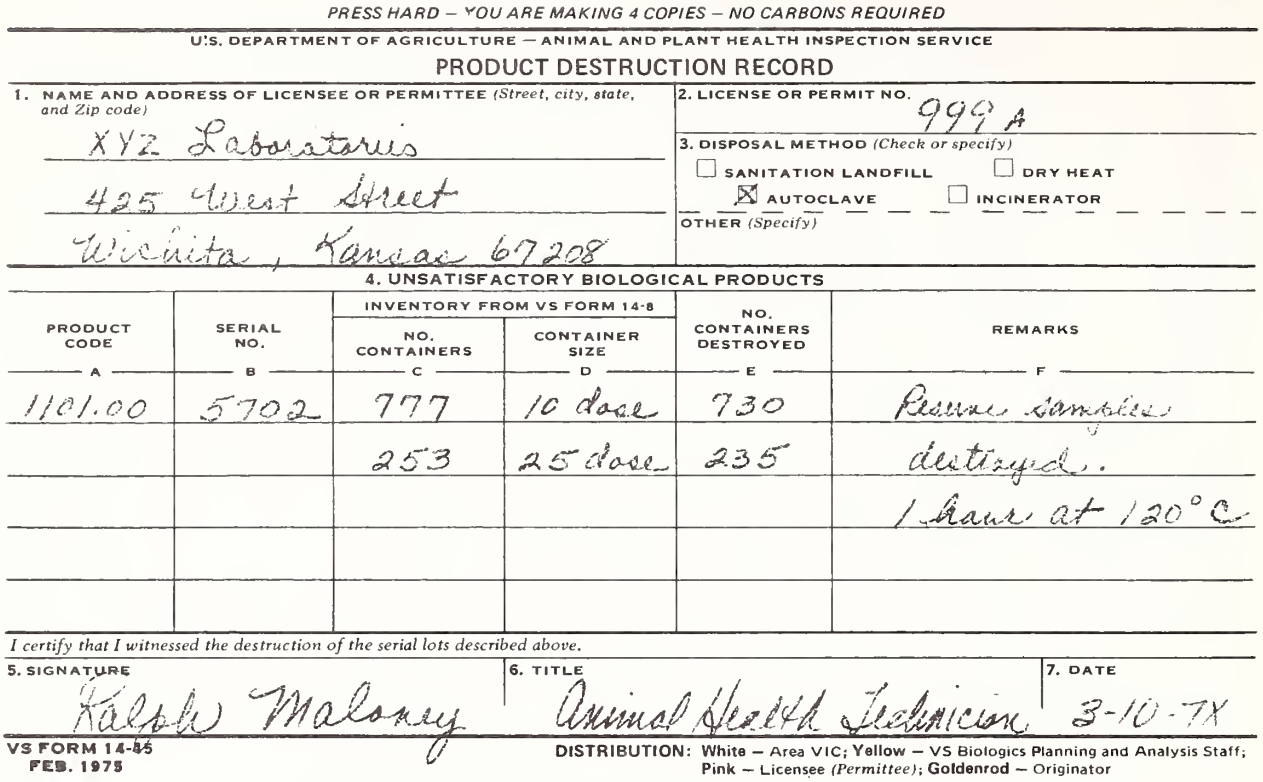
26. DATE RECEIVED

VS FORM 14-20
JULY 1975

REPLACES VS FORM 14-20 (5/73) WHICH MAY BE USED

AREA OFFICE

Figure 4-19



PRESS HARD — YOU ARE MAKING 4 COPIES — NO CARBONS REQUIRED

U.S. DEPARTMENT OF AGRICULTURE — ANIMAL AND PLANT HEALTH INSPECTION SERVICE

PRODUCT DESTRUCTION RECORD

1. NAME AND ADDRESS OF LICENSEE OR PERMITTEE *(Street, city, state, and Zip code)*

XYZ Laboratories
425 West Street
Wichita, Kansas 67208

2. LICENSE OR PERMIT NO. 999 A

3. DISPOSAL METHOD *(Check or specify)*

☐ SANITATION LANDFILL ☐ DRY HEAT
☒ AUTOCLAVE ☐ INCINERATOR

OTHER *(Specify)*

4. UNSATISFACTORY BIOLOGICAL PRODUCTS

PRODUCT CODE	SERIAL NO.	INVENTORY FROM VS FORM 14-8		NO. CONTAINERS DESTROYED	REMARKS
		NO. CONTAINERS	CONTAINER SIZE		
A	B	C	D	E	F
1101.00	5702	777	10 dose	730	Reserve samples
		253	25 dose	235	destroyed.
					1 hour at 120° C

I certify that I witnessed the destruction of the serial lots described above.

5. SIGNATURE Ralph Maloney

6. TITLE Animal Health Technician

7. DATE 3-10-7X

VS FORM 14-45
FEB. 1975

DISTRIBUTION: **White** — Area VIC; **Yellow** — VS Biologics Planning and Analysis Staff; **Pink** — Licensee *(Permittee)*; **Goldenrod** — Originator

Figure 4-21

DAILY INSPECTION NOTES

DATE OF VISIT: 10/2/76

REPORT OF VISIT TO COMMERCIAL FIRM BY USDA PERSONNEL

DAY: Tuesday

PAGE: 1 OF 6

FIRM: XYZ Labs

INSPECTOR: E. Ewell

EST. NO.: 999A

OTHERS: Spencer
Thompson
Kline

LOCATIONS VISITED:
2100 Edgemoor
425 West St.
XYZ Ranch

SUBJECT OF VISIT: In Depth

TIME SPENT AT FIRM: 7:45AM – 11:30AM
1:15pm – 3:45pm

PERSONNEL CONTACTED:
Dr Mark Sanborn - Lab Director
Dr. Jim Nodding - Head, Control
Mr. Mike Tyler - Prod. Super.
Ms. Carol Smith - Control Supervisor

BRIEF OUTLINE OF ACTIVITIES:
1 Meeting with Dr Sanborn
2. Tour of Facilities
3. Review of Licenses & Personnel List
4. Inventory of Shipping Cooler
5. Tour of Ranch

NOTES:

1. Carol Smith not on VS14-7 list. Newly employed. Requested Card be submitted.

2. Caps and stoppers noted under freezers in Bldg 10, Room A

3. Heavy Rains during visit to Ranch. Water drained rapidly from cattle yard. Apparently the drainage problem has been corrected.

PLEASE NUMBER, DATE, AND INITIAL ALL PAGES. SIGN THE LAST PAGE AND INDICATE DATE NOTES COMPLETED.

Figure 4-22

DAILY INSPECTION NOTES
CONTINUED:

EST. NO.: 999A PAGE: 2 OF 6
DATE: 10/2/7X INSPECTOR: EE

4. Discussed the inactive IBR and BVD licenses with Dr Sanborn. The single antigen product apparently does not sell very well. The IBR has been out of production since 1974 - 3 years - The firm wishes to retain the license one more year. We pointed out that the outline was outdated. Dr Sanborn agreed to revise the outline before producing any additional serials. The BVD license was last used in 1971 - over 5 years. Dr Sanborn gave us the license to return for termination.

Figure 4-23

INSPECTION

PRODUCT CHECK-OFF SHEET

Est. No.: 999A Page: 1 of 2

Product Code: 2401.00

Date: 10/4/7X Inspector: EE

Product Name: Clostridium Chauvoei-Septicum Bacterin

Outline Approved: 4-3-7X

Pages Revised: p 4-6 5/10/7X

SELECTED SERIALS

No. 1 No. 2 No. 3

Serial Number: 493

Seed Identification: chX2 chX14 Sept 23

Seed Lot No.: #47A #142B #399

Bulk Lot No.: 15 21 13

Inoculation Date: 11-5-74 1-6-75 10-2-74

Harvest Date/Amount: 11-9-74/10,000 ml 1-10-75/15,000 ml 10-6-74/4,000 ml

Pooling Date/Amt.: 2-6-75 / 20,000 ml

Filling Date/Size: Ⓐ 3-18-75/ 200 ml 3-20-75/100 ml

Filling Amount: 50 btls = 10,000 ml 100 btls = 10,000 ml

Label Date/Amount: 4-16/ 46 4-20/ 98

Expiration Date Check: 10-6-77 Label Copy OK

Sterility On/Off: 3-24/4-12 OK 3-24/4-12 OK

Potency On/Off: 2-8/3-15 OK

VS release by/Date: EE/4-18-76 EE/4-18-76

Firm release by/Date: gn/ 4-20 gn/4-20

Inventory from VS 14-8 50 X 200 ml 100 X 100 ml

Firms Inventory to Shipping: 45 X 200 ml 96 X 100 ml

OUTLINE CORRELATION:

1. Outline does not list the 200 ml size

2. Media formulation typographical error
Correct 5% NaHOH to 0.5% NaHOH

INSPECTION

PRODUCT CODE: 2401.00 PRODUCT CHECK-OFF SHEET CONTINUED EST. NO.: 999A PAGE: 2 OF 2

PRODUCT INSPECTION NOTES: DATE: 10/4/7X INSPECTOR: EE

1. Mix record is not accurate since the firm does not measure the exact amount put in storage Containers. They assume a standard amount per Container. Apparently the harvest size has increased and the result is a greater amount in each storage Container.

2. Fill records are not accurate since the recorded amount is the bottle size times number filled rather than the amount filled into each Container

3. Expiration has been accurately Calculated Labels on file for this serial show correct date printed.

E. Ewell
10/5/7X

POST INSPECTION ACTIVITIES

CONTENTS

Page
ESSENTIAL POST INSPECTION ACTIVITIES 33
Post Inspection Review and Critique 33
Writing the Report 33
The Letter to the Firm 34
Distribution of Report and Letter 35
Follow-up Inspections 35

POST INSPECTION ACTIVITIES

An inspection has not been properly completed until four post inspection activities have been finished.

ESSENTIAL POST INSPECTION ACTIVITIES

1. The team under direction of the Regional Biologics Specialist (RBS) meets, discusses, reviews, and consults with others concerning the inspection findings.
2. Each team member prepares his part of the report. Team members under the leadership of the RBS draft, assemble, critique, and issue a composite report of the inspection.
3. The RBS sends a letter to the firm listing exceptions found, arrangements for any corrections agreed upon, and sets dates for achieving compliance.
4. The RBS arranges follow-up inspections to determine compliance.

Post Inspection Review and Critique

An inspection will be viewed from a different perspective when the team returns to the Area Office...in an environment away from the establishment itself.

Reorganize all inspection notes and worksheets. These are the official legal records of the inspection. Be sure that (a) all pages are properly identified; (b) all sentences are complete; and (c) all meanings are clear. Be sure all exhibits or attachments have been identified.

Assemble notes and exhibits in a folder and identify the folder for easy retrieval at a later time. Place folder in a file that is secure and accessible only by authorized persons.

Prepare a summary report from your inspection notes.

Critique the inspection again. Go through each category examined. Carefully review again each exception found.

Be sure each exception is sufficiently documented.

Discuss each corrective action being required.

Consult with the Area Veterinarian in Charge (AVIC), the Regional Director, Biologics staff members, VSL personnel or others as appropriate.

Apply the three-question test to each action:
1. Is the action consistent with regulations?
2. Is the action consistent with VS policy?
3. Is it reasonable?

Inform the firm of subsequent decisions made after the wrap-up session at the plant.

Verify previous assignment of categories for report writing to each team member.

Begin writing.

Writing the Report

The inspection report must be:
1. Concise
2. Accurate
3. Comprehensive
   and a summary of significant events in the inspection.

Use VS Form 14-30, Field Inspection Report. See Figures 4-31 and 4-32.

Identify the team leader, all team members, and the assignment of each.

Assign each category to at least one team member.

Prepare a rough draft for categories examined during the inspection.

Examine again the pages in this manual entitled CATEGORIES OF INSPECTION. Note the categories and the checklist given in each category. Note the 9 CFR references given. Use these guidelines to prepare the report for the category.

Write concisely, clearly, and explicitly.

Apply this test to what you write! Will the report be clear to a U.S. attorney?

Use this format:

1. State what actually was done to investigate compliance for the category. Be explicit! Avoid general, vague statements! State quantities and methods used wherever possible.
2. State clearly the exceptions found.
3. Rate the exceptions as either (a) Serious, (b) Less Serious, (c) Minor.
4. Cite the applicable regulation violated for each exception found.
5. State the action required. Be specific. Phrases such as "use all necessary precautions" are too vague.
6. Specify the date action is to be completed. Do not use "immediately", this cannot be enforced.

Do not repeat descriptions of repeatedly noted exceptions. If recurring, so note.

Explain abbreviations by fully spelling out words later abbreviated when used the first time. Enclose the abbreviations in parentheses immediately following this first use.

Prepare and properly reference all attachments or appendices used.

Have the RBS edit the drafts and have team leader prepare the final report.

Prepare the report in the office where the files are. Do not rely on memory when citing file documents.

Distribute the final report for comments by team members and others concerned.

Check that all inspection notes, exhibits, and attachments have been assembled and are appropriately secured.

Be sure team leader signs and dates the report.

The Letter to the Firm

Within 10 days after completing the inspection, a letter must be prepared and sent to the firm describing inspection findings, needed corrective actions, and confirming actions taken and agreements made. Use the following guidelines:

State clearly and explicitly each exception that was found. Cite the regulation involved.

State each correction agreed upon for the exception found.

State the date compliance must be achieved for each agreed upon correction.

Include favorable comments.

Inform the firm if certain non-compliances have been referred to higher authorities for action.

Have the RBS prepare and sign the letter.

State that follow-up inspections will be scheduled to insure compliances, (if appropriate).

Avoid technical terms. If unavoidable, explain clearly. Identify all abbreviations with the full wording the first time used, e.g., Animal and Plant Health Inspection Service (APHIS). Other professional people not trained in biologics preparation such as lawyers may have to interpret the instructions in the letter.

Request a written reply from the licensee confirming that corrective actions have been completed.

Address the letter to an official with sufficient authority to insure corrective actions can be made.

Place the following statement at the end of the last page of the letter: "This is to certify the fore-going letter has been received, read, understood, and agreed to.

(name of licensee)
(company)

By (licensee official)

Date (date) 19XX"

Send by U.S. Mail using "Certified Mail with a return receipt request" when receipt by the licensee must be verified.

The RBS's responsibility for final preparation and distribution of the inspection report and the letter to the firm is given in VS Memo 800.3.

Distribution of Report and Letter

Prepare at least an original plus 4 copies of the VS Form 14-30 Inspection Report.

Send the original to the AVIC.

Send two copies to the Regional Director. The Regional Director will forward one copy to the Senior Staff Veterinarians Biologics Planning and Analysis Staff and one copy to the Senior Staff Veterinarians Biologics Licensing and Standards Staff.

Send one copy to Director, Veterinary Services Laboratories.

Keep one copy for the Regional Biologics Specialist files.

Attach a copy of the follow-up letter to each copy of VS Form 14-30 Report.

Follow-up Inspections

The detection of a non-compliance is only a start. Compliance is the desired end result.

Schedule follow-up inspections to determine if corrections have been made. Set tentative dates.

Prepare a follow-up list. Corrections can be identified and checked off as they are corrected.

Use the general inspection techniques in a follow-up that are used for an in-depth inspection. Modify them as needed to suit the circumstances.

Prepare a VS Form 14-30 Report for each follow-up inspection.

Figure 4-31

FIELD INSPECTION REPORT

PAGE 1 OF 2 PAGES

1. NAME OF FIRM & LOCATION OF PREMISES

XYZ Laboratories, Inc.
(a) 2100 Edgemoor Ave, Wichita, Kansas
(b) 425 West St., Wichita, Kansas
(c) XYZ Ranch, RR # 1, Duncan, Kansas

2. DATE(S) OF INSPECTION: Oct 2-10, 197X

3. ESTABLISHMENT LICENSE NO.: 999A

4. TYPE OF INSPECT.: In Depth

5. INSPECTION CATEGORIES (By Name)	6. FINDINGS
Inspection Team	E. Evell Regional Biologics Specialist Barbara Spencer Regional Biologics Specialist Judy Thompson Microbiologist Virology Section Veterinary Services Laboratory Erick Kline Biologics Compliance Officer
Purpose	Conduct an indepth inspection of this licensed establishment. We were requested by VSL to check methods of formalin determination and by BLSS to examine the proposed Rabies production facilities.
I. Personnel	A. The firm has established a system to review personnel forms every 3 months. The organization chart filed 3/20/74 is still accurate. Job Titles checked out accurately. The licensee noted their failure to report the hiring of Carol Smith as Control Supervisor (9CFR 114.7 - Minor).
ACTION	The licensee agreed to submit a VS Form 14-7 by Oct 12, 197X. The form was received in the Area Office Oct 10, 197X. Compliance Acheived.
	B. Employees appear to be well trained, adequate in number and show interest in their work. Dr Sanborn was observed examining incomming animals.

7. SIGNATURE (TEAM LEADER): E. EVELL

8. TITLE: Team Leader- Regional Biol. Spec.

9. DATE SIGNED: Oct. 18, 197X

VS FORM 14-30 PREVIOUS EDITION MAY BE USED

USDA-APHIS

Figure 4-32

CONTINUATION SHEET

FIELD INSPECTION REPORT

PAGE 2 OF 2 PAGES

1. NAME OF FIRM	2. LICENSE NO.	3. DATES OF INSPECTION	4. TYPE INSP.	5. TEAM LEADER
XYZ	999A	10/2 - 10/76	In Depth	Evell

6. INSPECTION CATEGORIES (BY NAME)	7. FINDINGS
II. Licenses	A. All items listed on the Est. Lic. were found to be accurate. Ownership is still in accord with the original application. The licensee is no longer producing IVR (Code 1101.00) and BVD (1201.00) as single antigen vaccines. The last serial of IBR was produced in 1974, but the licensee still wishes to retain the license. The license for BVD was presented to us to submit for termination. It was sent on to BLSS, Hyattsville by memorandum on Oct 12, 197X (copy attached).

VS FORM 14-30A

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 5
INVESTIGATION AND PROCESSING OF ALLEGED VIOLATIONS OF THE VIRUS-SERUM-TOXIN ACT

REGULATIONS FOR CHAPTER 5 WILL BE ISSUED LATER.

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 6
HANDLING OF CONSUMER COMPLAINTS INVOLVING BIOLOGICS

HANDLING OF CONSUMER COMPLAINTS

CONTENTS

Page
AUTHORITY FOR HANDLING CONSUMER COMPLAINTS 2
OBJECTIVES OF CONSUMER COMPLAINTS FOLLOW-UPS 2
HANDLING THE COMPLAINT 2
    Forwarding of Complaints 2
    Acknowledging the Complaint 2
    Assigning Case Number 2
    Preliminary Notice to Biologics Planning & Analysis Staff 2
    Gathering Facts 3
    Coordinating with VS Resource People 3
    VSL Testing 3
    Contacting Licensee 3
    Resolving the Complaint 3
QUESTIONNAIRE FOR GATHERING FACTS 3
CLOSING THE COMPLAINT FILE 3
    Letter to Complainant 3
    Follow-up Sheet 3
    Distribution of Reports 3
THE CENTRAL CONTROL FILE 3

HANDLING CONSUMER COMPLAINTS

AUTHORITY FOR HANDLING CONSUMER COMPLAINTS

The U.S. Department of Agriculture wants consumers to know they have the means to express to the Department complaints about products that are regulated by USDA. The Department has a consumer representation plan, the purpose of which "is to assure that the American consumers--the intermediate and ultimate recipients of the commodities, benefits and services administered by the Department of Agriculture--are well informed about Department actions affecting their interests, and that relevant Department decision-making processes are open to the effective expression of informed consumer viewpoints."

Consumer complaint policy for veterinary biologics is established in VS Memorandum 800.8.

OBJECTIVES OF CONSUMER COMPLAINTS FOLLOW-UPS

Follow-ups of consumer complaints involving biologics should accomplish three things:

Objectives

1. Provide prompt contact with complainant and lead to proper resolution of the complaint.
2. Accurately identify products allegedly involved, if possible.
3. Link related individual complaints so general problems may be recognized early.

HANDLING THE COMPLAINT

The following procedures should be carried out for each complaint:

Forwarding of Complaints

Be neutral and circumspect. Lawsuits are often involved. Your actions and opinions may be used by lawyers in court proceedings.

Be sure all complaints are rapidly made known to the Area Veterinarian in Charge (AVIC) in the Area in which the complainant resides. Tell him by phone if the urgency of the complaint warrants this type of action.

The AVIC, in turn, should ordinarily contact the Regional Biologics Specialist (RBS) for his Area. The RBS will then coordinate the resolution of the complaint.

Forward information you have about the complaint to the RBS or whomever the AVIC directs. Each complaint will be handled as the individual circumstances indicate.

The REGIONAL BIOLOGICS SPECIALIST will ordinarily handle each complaint as follows:

ACKNOWLEDGMENT

Acknowledge the complaint. If the initial acknowledgment is done by phone, send a letter confirming the call (Figure 6-5). If no further action is to be taken, explain why. If the case is going to be looked into further, tell the complainant that another letter will come later explaining VS findings.

Case Number

Get a case number from the AVIC for each case. Any local numbering system is okay if it has the following three things: (1) the fiscal year in which the complaint was received, (2) a unique accession number, and (3) identification as a complaint involving biologics. A complaint register may be used (Figure 6-7).

Preliminary Notice to Planning Staff

Notify the Biologics Planning and Analysis Staff (BPAS) that the complaint has been received immediately after assigning a case number. The VS Form 14-16 (Figure 6-8) or a phone call may be used. BPAS needs to have as much identification of the serial(s) involved as possible, the state where the complaint originated, the case number assigned, and a very short indication of the nature of the complaint. BPAS merges this information with other reports of complaints being processed and issues a monthly report of complaints being investigated.

Critical Facts

Gather all needed facts. To effectively check a complaint, at least the following information is needed: (1) the true name of the product, you can find this on the container label or on the carton, (avoid trade names); (2) the licensee look for the license number on the label if a label is available; and (3) the serial numbers of any lots allegedly involved. A useful questionnaire for gathering other information is presented in Figure 6-2.

Coordinate With VS Resource People

Use other VS resource people, if needed. If indicated, make arrangements with AVIC's, other Regional Biologics Specialists, Biologics Compliance Officers, Regional and Area Epidemiologists, District or Section VMO's to help gather facts.

VSL Testing

Contact VSL for testing or technical judgments, if indicated. Do not send any material or samples to VSL. First, contact the Head, Product Control Unit, VSL (FTS 862-8211) and discuss specific arrangements.

Document agreements with a VS Form 14-23 (Request for Testing) submission by mail. See Figure 6-1. Provide VSL with background on the case. VSL will ordinarily use samples from their Product Sample Repository rather than field samples.

Contacting Licensee

Contact the licensee. Ask for any information he may have concerning this or similar complaints. See Figure 6-6. If indicated, you may want to check out his complaint file on an inspection visit.

Resolving the Complaint

Resolve the complaint based upon the facts surrounding each complaint. Each case must be decided on its own merits. The case may be closed immediately due to insufficient information or grounds for complaint or it may require extensive investigation disclosing a critical problem.

QUESTIONNAIRE FOR GATHERING FACTS

The questionnaire in Figure 6-2 may help as a guide for gathering needed information.

CLOSING THE COMPLAINT FILE

A complaint is not closed until the findings are properly communicated to interested persons. This may include: (1) the complainant; (2) veterinary practitioners who assisted in the follow-up; (3) the licensee involved; (4) VS field personnel; (5) VS Staff personnel and (6) VSL.

Letter to Complainant

Summarize your findings in a letter to the complainant. Send a copy to any local veterinary practitioner who assisted in the follow-up. Send a letter to the licensee if you think the case warrants it.

Follow-up Sheet

Prepare a follow-up sheet (See Figure 6-3). Staple all documents to the follow-up sheet.

Distribution of Reports

1. Keep one set for the RBS file.
2. Send one set to each AVIC involved.
3. Send one set to VSL if testing was involved.
4. Send one set to the Biologics Planning and Analysis Staff in Hyattsville. Send this set through the Regional Director for his informtion also.

Try to close each complaint file within 90 days, if at all possible.

THE CENTRAL CONTROL FILE

A central file of all complaints processed provides a valuable source of information on various field problems being encountered with veterinary biologics.

The Biologics Planning and Analysis Staff (BPAS) will maintain this central control file.

File all completed complaint cases by fiscal year at BPAS.

Maintain and issue a list each month of biologics complaints completed or still in process, by case number. See Figure 6-4. If a case is more than 90 days old determine the reason and have BPAS give assistance in closing the case as soon as possible. Distribute this monthly report to Biologics Staffs, VSL, RBS's, and Regional Directors.

Tally numbers of complaints processed by fiscal year and use for reports concerning goals and accomplishments in BPAS budget work.

FIGURE 6-1

REQUEST FOR SPECIAL TESTING

INSTRUCTIONS FOR ORIGINATOR: Complete Items 1 thru 12. Send original and 5 copies with carbons intact to Director, Biologics Laboratories. Retain 7th copy.

1. ORIGINATOR *(Typed name)*

Dr. Edward Euell
Regional Biologics Specialist
Des Moines, Iowa

2. COMPANY *(Include address)*

XYZ Laboratories
Wichita, Kansas

3. LICENSE NO.

999A

4. PRODUCT

Bovine Rhinotracheitis Vaccine -
Leptospira Pomona Bacterin

5. SERIAL NO.

5364-4635

6. PRODUCT CODE

1119.00

7. PURPOSE OUTLINE CHANGE ☐ NEW PRODUCT ☐ TROUBLE CASE ☒ LICENSEE PROBLEM ☐

8. LICENSEE OR OTHER CONTACT *(Name of individual)*

9. SUPPORTING DATA ATTACHED YES ☐ NO ☒

10. REMARKS AND PRIORITY

This consumer complaint has been discussed with the section heads involved and with the head of Product Control, VSL. As agreed:

Request IBR titration with Leptospira Bacterin as Diluent.

Request Formalin determination on Leptospira Bacterin.

11. SIGNATURE OF ORIGINATOR

Edward Euell

Edward Euell, Regional Biologics Specialist

12. DATE SIGNED

February 17, 197X

INSTRUCTIONS FOR DIRECTOR, BIOLOGICS LABORATORIES: After Items 13 thru 15 are completed by Section Head, send original to Originator, duplicate to Biologics Planning and Analysis, triplicate to Area Veterinarian in Charge, and retain quadruplicate for your files.

13. ***REPLY BY SECTION HEAD***

14. SIGNATURE OF SECTION HEAD

15. DATE SIGNED

VS FORM 14-23
AUG. 1973

REPLACES VB FORM 23, APR. 1972, WHICH MAY BE USED.

USDA-APHIS

FIGURE 6-2
(1 of 4)

CONSUMER COMPLAINT
VS BIOLOGICS FIELD QUESTIONNAIRE

Accession Number

State	Program	FY	Case No.
CA	600	7X	003

Complainant: William Hamilton
Rt 3, Los Baños, California

Date of Report: 2-6-7X

Investigator: Ralph Spencer

Product Information:

Why Were Animals Vaccinated Routine part of herd Health Program

Product Name Bovine Rhinotrachitis Vaccine - Leptospira Pomona Bacterin
"BO - RHINO-LEP"

License Number of Producer 999A

How Much Purchased 500 doses - 50 dose bottles

Serial Number(s) 5364-4635

Expiration Date(s) 24 Sept 7X

Was Product Refrigerated When Received yes

Was Product Refrigerated Until Used yes

How Administered:

Species Involved Bovine

How Many Vaccinated 400 head

Date(s) of Vaccination Nov. 24 25, 197X

Route of Vaccination and Dose Administered 2cc I.M.

Site of Vaccination hip

Type of Syringe and Needles Used sterile plastic

Type of Sterilization of Equipment -none-

How Administered: (continued)

Antiseptic Used at Site of Inoculation none

Name of Vaccinator John Lester

Experience with Previous Vaccinations no problems - farm manager for 15 years

Reactions:

How Many Reacted Out of Total about 100

Reactions Started How Many Days After Vaccination one day

Number of Deaths over 20% in some groups

Deaths Started How Many Days After Vaccination 6 days

When Did Last Animal Die one month post vac.

Number That Recovered With After Effects Recovered showed poor performance

Symptoms:

Temperatures yes

Respiratory Symptoms labored breathing, runny noses

Appetites poor

Locomotion, Lameness, Unusual Movements sluggish

Diarrheas, Constipations, Etc. none

Reaction at Site of Inoculation none

Other Symptoms see post mortem

Post Mortem Results:

How Many Posted 4

How Long After Death within 12 hr

Posted By Dr. S. Churchill (local practitioner - vet)

Post Mortem Results: (continued)

Describe Findings Lung lesions characteristic of Pasturella / Haemophilus
Trachea showed catarrhal dammage suggestive of IBR Complex

Tissues Examined Liver, Lung, Trachea

Name & Address of Laboratory (attach report if possible) Serology IBR Isolated
California Vet Med Diag. Lab
Box 5020, Sacramento, CA 95320

Husbandry Practices:

Where Kept 21 Days Prior to Vaccination Lot 169 11/23/7X from Montana

Where Kept After Vaccination feed yard

Weather Conditions (if applicable):

Before Vaccination ✓ nothing unusual

After Vaccination ✓

Any Other Unusual Stresses no

Feeding 21 Days Prior to Vaccination Range

Feeding After Vaccination Hay, Starter grain

Treatment(s) (if any):

Medication(s) Prior to Vaccination unknown

Medication(s) After Symptoms Showing Broad spectrum antibiotics
Sulfa

Effect of Medication (if any) erratic

Pesticide(s) Used on Animals or Premises none

Surgery none

Who Prescribed (if applicable)

S Churchill DVM

CONSUMER COMPLAINT VS BIOLOGICS FIELD QUESTIONNAIRE

FIGURE 6-2
(4 of 4)

Any Other Information:

Chemicals, Contamination of Water Supply, Other

None

Comments:

Cattle were vaccinated on the second day after shipping from Montana. The first signs of respiratory disease occured the day after vaccination with deaths about 5 days later

Source(s) of Information Obtained by:

Phone

[✓ Personal Visit]

Other (specify)

Signed Ralph Spencer, VMO

Date 2-6-7X

FIGURE 6-3

VS BIOLOGICS CONSUMER COMPLAINT FOLLOWUP SHEET

Name of the Regional Biologics Specialist Eward Euell Area Number 18

	State	Program	FY	Case Number
Accession No.	CA	600	7X	003

Product Involved: IBR Vaccine-Lepto Bacterin

Produced by: XYZ Lab Lic 999A

Serial No. (if known): 5364-4635

Ledger Information:

Complainant's Name & Address

William Hamilton

Veterinarian's Name & Address

Stuart Churchill DVM
Los Banos, California

Brief Description of Problem: 20 - 25% morbidity and mortality
Lab isolated IBR

Chronology of Events

Date	Action	By
2/2/7X	Complaint Received (attach copy incoming)	Euell
2/2/7X	Complaint Acknowledged (attach copy)	Euell
2/9/7X	Licensee Contacted (attach copy) Called J.B. Taft for VS 14-8's and VS14-14 s	Euell
2/17/7X	VSL Testing Requested (attach VS14-23 & VSL Report)	Euell
2/6/7X	Field Investigation Made (attach copy)	RALPH SPENCER
4/12/7X	Final Report to Complainant (attach copy)	Euell
4/12/7X	Final Report to Licensee (attach copy)	Euell
4/12/7X	Case Closed	Euell
	Other (specified, attach copy)	

Figure 6-4

MONTHLY REPORT OF CONSUMER COMPLAINTS INVOLVING VETERINARY BIOLOGICS Report No. 20 Date ________ Page____

State Where Originated	Regional Biologics Specialist	Product Number and Name	Licensee No. and Name	Serial No.	Case No.	Date Originated	Date BPAS Notified	In Process	New	Closed Date	Comments
CA	Euell	1119.00 IBR-Lepto Pomona Bact.	XYZ Labs	5364-4635	7X-02-03	2/10/7X	2/21/7X		X		IBR break in calves
MN	Peterson	2702.13 Past. Mult. Bact. Av Isolates Types 1, 3 &4	Phoenix Labs	116A	001	1/15/7X	2/2/7X		X		Swelling in inoc. site
IL	Belini	1311.20 Distemper-Hepatits Vac. MLV,CLO	Premium Labs	249	7X-005	12/2/7X	1/15/7X			2/8/7X	Blue eyes in pups

BPAS

Distribution: Licensing & Standards (Dr. Price)
Veterinary Services Laboratory (Dr. Goff)
Regional Directors
Regional Biologics Specialists

(After a case has been shown as "closed" it will be dropped from future reports. A case is shown as "new" when first appearing on this report and will be carried as "in process" until "closed.")

FIGURE 6-5

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY SERVICES
210 WALNUT STREET, ROOM 877
DES MOINES, IOWA 50309

February 2, 197X

Steven Churchill, D.V.M.
R.R. 3
Los Banos, CA 79321

Dear Dr. Churchill:

This acknowledges receipt of your Veterinary Biologics Consumer Complaint regarding the deaths and illness of feeder cattle following vaccination with XYZ Laboratories' Bo-Rhino-Lep (Bovine Rhinotracheitis Vaccine - Leptospira Pomona Bacterin), Serial 5394-4635.

We have initiated an investigation of this matter and will keep you informed of our findings.

Sincerely,

Edward Euell

Edward Euell
Regional Biologics Specialist

cc:
AVIC
Complaint File

FIGURE 6-6

REPORT OF CONSUMER COMPLAINT TO THE LICENSEE

ACCESSION NO. CA-600-7X-003

FIRM XYZ Laboratories

DATE OF REPORT February 9, 197X

CODE 1119.00

SERIAL NO. 5394-4635

LICENSE NO. 999X

TRADE NAME Bo-Rhino-Lep

TRUE NAME Bovine Rhinotracheitis Vaccine - Leptospira Pomona Bacterin

NO. DOSES PRODUCED THIS SERIAL 21,000

COMPLAINANT'S NAME William Hamilton

PHONE NO. (707)465-3981

ADDRESS Los Banos, California

VETERINARIAN Dr. S. Churchill

PHONE NO. (707)465-3847

ADDRESS Los Banos, California

BRIEF DESCRIPTION OF PROBLEM

20 percent of a heard of 400 feeder cattle showed signs of respiratory infections 14 to 60 days after vaccination. Approximately 45 dead.

Edward Ewell
Regional Biologics Specialist

OTHER FIELD COMPLAINTS THIS SERIAL (PLEASE ATTACH)

FIRM CONTACTED COMPLAINT ____________ RESULTS ____________

RESULTS OF LICENSEE'S INVESTIGATION (PLEASE ATTACH ADDITIONAL RESULTS IF ANY)

CONCLUSIONS

____
Signature Firm Representative

FIGURE 6-7

FIELD COMPLAINT REGISTER

CASE NUMBER & DATE RECEIVED	NAME & ADDRESS OF COMPLAINANT	PRODUCT NAME LICENSEE & SERIAL	TYPE OF ACTION & DATE	FOLLOW-UP AS INDICATED & DATE	REMARKS
CA 600-7X-003 2-2-7X	S. CHURCHILL, DVM LOS BANOS, CA W. HAMILTON LOS BANOS, CA	IBR-LEPTO (PACKAGE) 5394-4635 XYZ LABS-999A	ACKNOW-2-2-7X	FIELD REPORT 2-6-7X LICENSEE NOTIFIED 2-9-7X	DSM AREA - BIO 7X-012 CASE CLOSED 2-12-7X

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINANY SERVICES
BIOLOGICS PROGRAM

ADDITIONAL VETERINARY BIOLOGICS SERIAL INFORMATION

TO: Biologics Data Center
Biologics Planning and Analysis Staff
Veterinary Services, APHIS - USDA, Ward Plaza
P.O. Box 844
Ames, Iowa

FIGURE 6-8

PRODUCT CODE 1119.00	LICENSE NO. 999A	SERIAL NO. 5364-4635

ADD THE FOLLOWING INFORMATION TO THE DATA BASE FOR THE ABOVE SERIAL

114.18 ☐ A. Date this serial was approved for reprocessing ____.
New serial number assigned ____

114.17 ☐ B. Date this serial was approved for rebottling ____.
New serial number assigned ____

114.14 ☐ C. Date this serial was approved for extension of dating ____.
Old expiration date ____ New expiration date ____.
Number of doses redated ____.

113.98 ☐ D. This serial of Autogenous Bacterin exceeds the limitations of 9 CFR 113.98, with this exception ____

Date exception was approved ____.

114.15 ☐ E. This serial, found unsatisfactory by Veterinary Services Laboratories, was destroyed under one of our employees' supervision. Date of disposal ____.

☐ F. This serial was not processed for release as recommended by Product Control, Veterinary Services Laboratory, based on data not available to them at the time of recommendation.
Date of action ____ Type of action ____.
Comments ____

☐ G. The release of this serial was held up at the area office due to ____
____. Actual release date ____

☒ H. The following information should be noted in the data base for this serial *(investigations, consumer complaints, all other)* CONSUMER COMPLAINT CA-600-7X-003

S. CHURCHILL
LOS BANOS, CA

FEEDER CATTLE
MORBIDITY AND MORTALITY
IBR ISOLATED

SIGNATURE OF REPORTING INDIVIDUAL	TITLE	DATE
Eward Enell	Regional Biologics Spec.	2-2-7X

VS FORM 14-16
OCT. 1974

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 7
PRODUCT RELEASE/OTHER AREA OFFICE PROCEDURES

REGULATIONS FOR CHAPTER 7 WILL BE ISSUED LATER.

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 8
PRODUCT SAMPLING

PRODUCT SAMPLING

CONTENTS

Page
AUTHORITY FOR SAMPLING.......... 2
PRESAMPLING ACTIVITIES.......... 2
SELECTING SAMPLES.......... 2
    Final Container Samples.......... 2
    Bulk Samples.......... 2
    Alternate Inventory Verification Method.......... 3
PROPER IDENTIFICATION AND DOCUMENTATION.......... 3
    Sample Labels.......... 3
    VS Form 14-20.......... 4
TAMPER-PROOFING OF SAMPLES.......... 4
    Proper Packing.......... 4
    Initials on Sealing Tape.......... 4
RESERVE SAMPLES.......... 4
SAMPLER ROSTER.......... 5
TRAINING OF SAMPLERS.......... 5

PRODUCT SAMPLING

Authority for Sampling

The authority for selection of samples to be (1) shipped to Veterinary Services Laboratories and (2) held by the vaccine producer in reserve is contained in 9 CFR 113.3(a) and (c). The number of samples to be taken is prescribed in 9 CFR 113.3(b) or in the outline of production. When the number is specified in the outline, this takes precedence over the number prescribed in 9 CFR 113.3(b). The number of samples taken is doubled when the samples are to be used in prelicensing evaluation or for outline changes (9 CFR 113.3(b)(8). The number of reserve samples to be taken is specified in 9 CFR 113.3(c)(1).

PRESAMPLING ACTIVITIES

Collection of biologics samples is supervised by the Section Veterinary Medical Officer (VS Memo 800.2). The individual sampler should:

> Review 9 CFR 113.3 and the Outlines of Productions to be sure you know the correct number of samples required for each product licensed for the firms you are visiting.
>
> Check that you have a valid USDA identification card or other identification to be able to verify to the licensee that you are an employee or authorized contractor of VS.
>
> Arrange with each licensee to supply a clean laboratory coat or similar protective clothing to you. Wear this at all times when you are carrying out your duties. If accidentally contaminated or soiled, change and have licensee decontaminate it as they do other similar protective clothing. Laboratory clothing should not be removed from the premises.
>
> Observe all vector control rules of the licensee at all times. Review RULES OF CONDUCT in Section 4-14 of the manual occasionally so they will be well known to you.
>
> Verify by phone or other means that at least 3 serials will be ready for sampling. This "three serial" guideline is not meant in any way to create a hardship upon the licensees who have products needing urgent sampling. There are, however, ways that fewer visits can be worked out with the licensee, thereby making sampling visits more productive and less costly.

Product Sampling can be divided into 3 major tasks: (1) Selection of samples, (2) Proper identification of samples (including checking of accompanying documentations) and (3) Tamper-proofing of samples.

SELECTING SAMPLES

Keep the samples under constant surveillance. If necessary to leave them at any time before tamper-proofing, place them in a sealed or locked container or in a locked or sealed storage area. Procedures are different for taking (1) final container and (2) bulk samples.

There is a difference between random sampling and representative sampling. Random sampling is a statistical technique in which each and every container in the serial has an equal chance of being selected. Chance alone operates. Biologics sampling is representative sampling. For reasons of time and cost, selection is made using a plan in which judgment factors in addition to chance, are involved. For this reason, biologics sampling is not truly random.

Final Container Samples	Be sure the entire serial or subserial is presented for sampling. If there are reasons to believe the entire serial has not been presented, ask for the filling records and verify quantities.
	Pick from several storage containers to get a representative sampling that represents different filling periods.
	Include all container sizes in representative proportions.
	Avoid using set patterns in which cartons in the same relative locations or containers in the same relative location within a carton are selected repeatedly. On occasion, require that ordinarily inaccessible cartons be moved so they also may be sampled.

Hold samples from each serial or subserial separate until tamper-proofed.

Be sure correct labels are applied to each container.

Occasionally, bulk samples of completed product may be selected for testing as directed by the District Veterinarian.

Bulk Samples

Be sure the entire serial has been presented for sampling. If there are reasons to believe the entire serial has not been presented, ask for the bulk mixing records and verify quantities.

Check the outline of production and 9 CFR to be sure submission of bulk samples is permitted.

Verify the identification of the serial by checking tags, labels, or other markings on the tank or container in which the bulk product is held.

Insist that agitators in the tanks or containers are started up and allowed to operate for enough time to insure the product is completely mixed and uniform.

Watch the samples being taken. If you do not observe the actual sampling, the samples are not authentic and you cannot certify so in VS Form 14-20, Block 19. If it is authorized by your District Veterinarian, try to arrange your schedule with the firm so you can observe as many of the bulk samples being taken as possible. If an authenticated bulk sample is needed, you must be present.

Alternate Inventory Verification Method

In lieu of presenting filling records and bulk mixing records for each serial, the licensee may provide a summary of this information to help the sampler verify that all inventory has been presented for sampling. A suggested format is shown in Figure 8-5. If this method is used by the licensee, the sampler should do the following:

Have the licensee retain a copy of this summary as part of the production record. These summaries can be later used by VS inspectors during audits of serial records.

PROPER IDENTIFICATION AND DOCUMENTATION

Each sample must be properly labeled and its identity correctly linked with accompanying paperwork so testing results obtained from the samples actually reflect the serial from which the samples were taken.

Sample Labels

Check each sample label for errors or omissions. Essential information is as follows:

Producer's Name & License Number

True Name of Product (may be abbreviated)

Serial or Subserial Number

Amount in the Container (in cc's, ml's, or units)

Dose Size (in cc's, ml's, or units).

Most firms use approved printed labels on samples of licensed products in final container. But other labels are permissible. With the exception of the license number, all essential information must appear on a label for a prelicensing sample.

Check all labels for legibility and durability. If partially or completely illegible, or easily removed by rubbing, report this fact immediately to your Section Veterinarian or Regional Biologics Specialist for action.

A completed VS Form 14-20 SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES must accompany each shipment of samples (See Figures 8-1, 8-2, and 8-3). The licensee completes all portions of the form except Blocks 19-23.

VS Form 14-20

Check the VS Form 14-20 for omissions and errors.

Separate 14-20's must be used for any one or any combination of the following three groups: See Block 4. They must be clearly marked as to which group is being submitted.

Group 1. Routine Concurrent Samples - includes both bulk and final container samples. and/or

Retention Samples - for autogenous bacterins only. and/or

Resubmissions - for additional samples submitted in response to VSL requests or other circumstances. See Figure 8-1.

Group 2. Prelicensing Samples - includes both prelicensing and outline change samples. See Figure 8-2.

Group 3. Other - for master seed stocks, stock cultures, serums, etc. See Figure 8-3.

Check to be sure that the data appearing on the label and on the 14-20 (Blocks 6-15) agree.

Draw a line through the blank spaces in Blocks 6-15.

TAMPER-PROOFING OF SAMPLES

Tamper-proofing involves placing samples in cartons and subsequently sealing the cartons so they cannot be opened or the contents disturbed without it being obvious to Veterinary Services Laboratories at receipt.

Proper Packing

Insure that the authenticated samples can be handled properly in accordance with 42 CFR 72-25(b) (Figure 8-4). Note that samples are to be "packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation". Special care should be taken to prevent breakage of glass containers. All vials, glass or plastic, should be packed in nested cartons or by other methods commonly used when shipping to distributors or consumers.

Remember that leakage of liquid from a carton may mean refusal by a common carrier to handle it. Damaged shipments may be destroyed by VSL personnel upon receipt at the VSL Samples Repository.

Initials on Sealing Tamper-Proofing

Place initials or signatures across tape around nesting cartons and across tapes and surface of shipping cartons. Inked stamps are unacceptable.

Return tamper-proofed shipping cartons to licensee. The licensee is responsible for actual shipment of samples to VSL. The correct address of the VSL Samples Repository is:

Product Control Unit
Veterinary Services Laboratory, APHIS, USDA
P. O. Box 844, 700 S. Duff Avenue
Ames, IA 50010

RESERVE SAMPLES

Reserve samples are held on the licensee's premises for government use if needed. They must be tamper-proofed separately from the other serials or subserials.

See that authenticated reserve samples are given to the firm for storage in a secure area.

Return reserve samples to the firm at 6 months after the expiration date for the serial or subserial.

SAMPLER ROSTER

The Product Control Unit, VSL, maintains a file of the names of current samplers, their addresses, the establishments where they pick up samples, and specimens of their signatures, and the initials they use to tamper-proof cartons. Copies of VSL requests to samplers to resample selected serials are sent to the addresses shown in this file. It is therefore important that the AVIC or other responsible person do the following:

> Submit promptly to the Director, Veterinary Services Laboratories, any additions, deletions, or changes to the roster of samplers. Make sure the letter shows the correct name, address, and establishment assignments of the samplers and a specimen of their signature and initials.

TRAINING OF SAMPLERS

The Regional Biologics Specialist (RBS) has been assigned to each Area in which biologics sampling is being done. The RBS trains, advises, and instructs VS employees and contractors in the methods, procedures, and policies used in biologics sampling.

> Contact your RBS through the AVIC if you have questions involving sampling or if training or review of sampling activities is required.

FIGURE 8-1

FORM APPROVED: OMB NO. 40-R3460

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES

INSTRUCTIONS: Submit original and one copy with samples. **(Leave First Carbon Intact.)**

1. DATE SUBMITTED: 3-27-7X

2. FIRM LICENSE NO.: 999A

3. NAME AND MAILING ADDRESS OF FIRM *(Include Zip Code)*

XYZ Laboratories
P.O. Box 762
Wichita, KS 67208

4. PURPOSE
ROUTINE CONCURRENT SAMPLE ☒ PRELICENSING SAMPLE ☐
RETENTION SAMPLE ☐ RESUBMISSION ☐ *(Specify in remarks)* OTHER ☐ *(Specify in remarks)*

5. HOW IS PRODUCT SHIPPED
DRY ICE ☐ WATER-ICED ☒ UNREFRIGERATED ☐

OTHER *(Specify)*

PRODUCT IS SHIPPED VIA: United Parcel Service

PRODUCT NAME 6	PRODUCT CODE 7	SERIAL NO. 8	SAMPLE CODE *(For Gov't Use Only)* 9	HARVEST DATE 10	EXPIRATION DATE 11	SAMPLE CONTAINERS SUBMITTED NO. 12	SIZE 13	FIELD DOSE 14	INDICATE BULK OR FINAL 15
Clostridium Chauvoei Septicum Bacterin	2401.00	1313		3-1-7X	3-1-7Y	13	50D 250CC	5CC	Final
Autogenous Bacterin Lapine Isolates-Aqueous	2051.03	421		3-2-7X	9-2-7X	2	50CC in 250's		
Clostridium Chauvoei Septicum Bacterin	2401.00	** 1312		2-28-7X	2-28-7Y	20	50D 250CC	5CC	Final
Erysipelothrix Rhusiopathiae Bacterin	2461.20	258		2-23-7X	2-23-7W	2	50D 100CC	2CC	Bulk

16. REMARKS
**Per request of Dr. Freeman dated 3-25-7X
Resubmission

17. IF THIS FORM IS NOT USED TO AUTHENTICATE SAMPLES ATTACH COPIES OF ALTERNATE FORMS FOR ALL SERIALS LISTED ABOVE.

18. SIGNATURE OF FIRM REPRESENTATIVE
Mark C. Sanborn DVM
4-1-7X

FOR OFFICIAL GOVERNMENT SAMPLER

19. NUMBER OF SERIALS SAMPLED AND LISTED ON THIS PAGE: 2

20. REMARKS: Serial 421 and 258 not authenticated. Other samples packaged, sealed with tape and initialed (RM), dated 3-27-7X

21. SIGNATURE: Ralph Maloney

22. TITLE: Animal Health Tech

23. DATE: 3-27-7X

ACKNOWLEDGEMENT OF RECEIPT OF SAMPLES

24. CONDITION AND REMARKS

25. RECEIVED BY *(Signature)*

26. DATE RECEIVED

VS FORM 14-20
JULY 1975

FORM 14-20 (5/73) WHICH MAY BE USED

SUBMIT WITH SAMPLES

FIGURE 8-2

FORM APPROVED: OMB NO. 40-R3460

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES

1. DATE SUBMITTED 4-1-7X

2. FIRM LICENSE NO. 999A

3. NAME AND MAILING ADDRESS OF FIRM *(Include Zip Code)*

XYZ Laboratories
P.O. Box 762
Wichita, KS 67208

INSTRUCTIONS: Submit original and one copy with samples. **(Leave First Carbon Intact.)**

4. PURPOSE
ROUTINE CONCURRENT SAMPLE ☐ PRELICENSING SAMPLE ☒
RETENTION SAMPLE ☐ RESUBMISSION ☐ *(Specify in remarks)* OTHER ☐ *(Specify in remarks)*

5. HOW IS PRODUCT SHIPPED
DRY ICE ☐ WATER-ICED ☐ UNREFRIGERATED ☒

OTHER *(Specify)*

PRODUCT IS SHIPPED VIA Air Mail

PRODUCT NAME 6	PRODUCT CODE 7	SERIAL NO. 8	SAMPLE CODE *(For Gov't Use Only)* 9	HARVEST DATE 10	EXPIRATION DATE 11	SAMPLE CONTAINERS SUBMITTED NO. 12	SAMPLE CONTAINERS SUBMITTED SIZE 13	SAMPLE CONTAINERS SUBMITTED FIELD DOSE 14	INDICATE BULK OR FINAL 15
Pasteurella Multocida Antiserum Bovine Isolates,	3701.00	123		3-30-7X	-	24	100CC - 10D	10CC	
Bovine Origin	3701.00	124		3-30-7X	-	24	100CC - 10D	10CC	
	3701.00	125		3-30-7X	-	24	100CC - 10D	10CC	

16. REMARKS
Per VS 14-23 by Dr. Turner dated 3-15-7X

17. IF THIS FORM IS NOT USED TO AUTHENTICATE SAMPLES ATTACH COPIES OF ALTERNATE FORMS FOR ALL SERIALS LISTED ABOVE.

18. SIGNATURE OF FIRM REPRESENTATIVE Mark C. Sanborn
Mark C. Sanborn
Mark C. Sanborn DVM 4-1-7X

FOR OFFICIAL GOVERNMENT SAMPLER

19. NUMBER OF SERIALS SAMPLED AND LISTED ON THIS PAGE 3

20. REMARKS Boxes sealed, taped, and initialed by me 4-1-7X

21. SIGNATURE Ralph Maloney

22. TITLE Animal Health Tech

23. DATE 4-1-7X

ACKNOWLEDGEMENT OF RECEIPT OF SAMPLES

24. CONDITION AND REMARKS

25. RECEIVED BY *(Signature)*

26. DATE RECEIVED

VS FORM 14-20
JULY 1975

REPLACES VS FORM 14-20 (5/73) WHICH MAY BE USED

SUBMIT WITH SAMPLES

FIGURE 8-3

FORM APPROVED: OMB NO. 40-R3460

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

SHIPMENT AND RECEIPT OF BIOLOGICS SAMPLES

1. DATE SUBMITTED 4-1-7X

2. FIRM LICENSE NO. 999A

3. NAME AND MAILING ADDRESS OF FIRM *(Include Zip Code)*

XYZ Laboratories
P.O. Box 762
Wichita, KS 67208

INSTRUCTIONS: Submit original and one copy with samples. **(Leave First Carbon Intact.)**

4. PURPOSE
ROUTINE CONCURRENT SAMPLE ☐ PRELICENSING SAMPLE ☐
RETENTION SAMPLE ☐ RESUBMISSION ☐ *(Specify in remarks)* OTHER ☒ *(Specify in remarks)*

5. HOW IS PRODUCT SHIPPED
DRY ICE ☒ WATER-ICED ☐ UNREFRIGERATED ☐

OTHER *(Specify)*

PRODUCT IS SHIPPED VIA Air Freight

PRODUCT NAME 6	PRODUCT CODE 7	SERIAL NO. 8	SAMPLE CODE *(For Gov't Use Only)* 9	HARVEST DATE 10	EXPIRATION DATE 11	SAMPLE CONTAINERS SUBMITTED NO. 12	SAMPLE CONTAINERS SUBMITTED SIZE 13	SAMPLE CONTAINERS SUBMITTED FIELD DOSE 14	INDICATE BULK OR FINAL 15
Bovine Virus Diarrhea Master Seed Virus	1201.00	7X-5		3-10-7X	-	15			

16. REMARKS

VS 14-23 by Dr. Turner dated 2-18-7X

17. IF THIS FORM IS NOT USED TO AUTHENTICATE SAMPLES ATTACH COPIES OF ALTERNATE FORMS FOR ALL SERIALS LISTED ABOVE.

18. SIGNATURE OF FIRM REPRESENTATIVE Mark C. Sanborn
Mark C. Sanborn
Mark C. Sanborn DVM 4-1-7X

FOR OFFICIAL GOVERNMENT SAMPLER

19. NUMBER OF SERIALS SAMPLED AND LISTED ON THIS PAGE 1

20. REMARKS Master Seed not authenticated

21. SIGNATURE Ralph Maloney

22. TITLE Animal Health Tech

23. DATE 3-31-7X

ACKNOWLEDGEMENT OF RECEIPT OF SAMPLES

24. CONDITION AND REMARKS

25. RECEIVED BY *(Signature)*

26. DATE RECEIVED

VS FORM 14-20
JULY 1975

REPLACES VS FORM 14-20 (5/73) WHICH MAY BE USED

SUBMIT WITH SAMPLES

(r) *Shellfish.* Any fresh, frozen, or incompletely cooked oysters, clams, or mussels, either shucked or in the shell, and any fresh, frozen, or incompletely cooked edible products thereof.

[21 F.R. 9881, Dec. 12, 1956, as amended at 25 F.R. 43, Jan. 5, 1960; 27 F.R. 2152, Mar. 6, 1962; 36 F.R. 11025, June 8, 1971]

Subpart B [Reserved]

Subpart C—Shipment of Certain Things

§ 72.25 Etiologic agents.[1]

(a) *Definitions.* As used in this section:

(1) An "etiologic agent" means a viable microorganism or its toxin which causes, or may cause, human disease.

(2) A "diagnostic specimen" means any human or animal material including, but not limited to, excreta, secreta, blood and its components, tissue, and tissue fluids being shipped for purposes of diagnosis.

(3) A "biological product" means a biological product prepared and manufactured in accordance with the provisions of 9 CFR Part 10, Licensed Veterinary Biological Products, 42 CFR Part 73, Licensed Human Biological Products, 21 CFR 130.3, *New drugs for investigational use in humans,* 9 CFR Part 103, Biological Products for Experimental Treatment of Animals, or 21 CFR 130.3(a), *New drugs for investigational use in animals,* and which, in accordance with such provisions, may be shipped in interstate traffic.

(b) *Transportation; etiologic agent minimum packaging requirements.* No person may knowingly transport or cause to be transported in interstate traffic, directly or indirectly any material, including but not limited to, diagnostic specimens and biological products, containing, or reasonably believed by such person to contain, an etiologic agent unless such material is packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation.

(c) *Transportation; etiologic agents subject to additional requirements.* No person may knowingly transport or cause to be transported in interstate traffic, directly or indirectly, any material, other than diagnostic specimens and biological products, containing, or reasonably believed by such person to contain, one or more of the following etiologic agents unless such material is packaged in accordance with the requirements specified in paragraph (b) of this section, and unless, in addition, such material is packaged and shipped in accordance with the requirements specified in subparagraphs (1)-(6) of this paragraph:

BACTERIAL AGENTS

Actinobacillus—all species.
Arizona hinshawii—all serotypes.
Bacillus anthracis.
Bartonella—all species.
Bordetella—all species.
Borrelia recurrentis, B. vincenti.
Brucella—all species.
Clostridium botulinum, Cl. chauvoei, Cl. haemolyticum, Cl. histolyticum, Cl. novyi, Cl. septicum, Cl. tetani.
Corynebacterium diphtheriae C, equi, C. haemolyticum, C. pseudotuberculosis, C. pyogenes, C. renale.
Diplococcus (Streptococcus) pneumoniae.
Erysipelothrix insidiosa.
Escherichia coli, all enteropathogenic serotypes.
Francisella (Pasteurella) tularensis.
Haemophilus ducreyi, H. influenzae.
Herellea vaginicola.
Klebsiella—all species and all serotypes.
Leptospira interrogans—all serotypes.
Listeria—all species.
Mima polymorpha.
Moraxella—all species.
Mycobacterium—all species.
Mycoplasma—all species.
Neisseria gonorrhoeae, N. meningitidis.
Pasteurella—all species.
Pseudomonas pseudomallei.
Salmonella—all species and all serotypes.
Shigella—all species and all serotypes.
Sphaerophorus necrophorus.
Staphylococcus aureus.
Streptobacillus moniliformis.
Streptococcus pyogenes.
Treponema careteum, T. pallidum, and *T. pertenue.*
Vibrio fetus, V. comma, including biotype El Tor, and *V. parahemolyticus.*
Yersenia (Pasteurella) pestis.

FUNGAL AGENTS

Actinomycetes (including *Nocardia* species, *Actinomyces* species and *Arachnia propionica*).
Blastomyces dermatitidis.
Coccidioides immitis.
Cryptococcus neoformans.
Histoplasma capsulatum.
Paracoccidioides brasiliensis.

---

[1] The requirements of this section are in addition to and not in lieu of any other packaging or other requirements for the transportation of etiologic agents in interstate traffic prescribed by the Department of Transportation and other agencies of the Federal Government.

SAMPLE COLLECTION FORM

FIGURE 8-5

LICENSE NUMBER:

FIRM NAME XYZ Laboratories

DATE SAMPLES COLLECTED 3/27/7X

IDENTIFICATION			INVENTORY			SAMPLE DATA 9 CFR 113.3			FOR SAMPLER'S USE			
PRODUCT NAME	PRODUCT CODE	SERIAL NUMBER	CONTAINER SIZE	NO. OF CONTAINERS	No. Storage CONTS	TEST SAMPLES	RESERVE SAMPLES	TOTAL COLLECTED				
CCS	2401.00	1312	100cc	1000	10	13	2	15	30%	7 + 2		
			250cc	800	10				40%	5		
			500 cc	200	10				10%	1		
				2000								
CCSP	2461.00	1703	250cc	800	10	15	2	17	88%	13 + 2		
			500cc	100	5				12%	2		
				900								
IBR	1151.00	2079	10 dose	4,000	10	16	2	18	75%	12 + 2		
			20 dose	789	6				15%	2		
			50 dose	366	10				10%	2		
				5155								
IBR-BVD-PI3	1171.00	3593	25 dose	4,072	14	16	2	18	70%	11 + 2		
			50 dose	1,698	16				30%	5		
				5770								
Rabies	1901.11	4932	1 dose	25,276	12	16	5	21	100%	16 + 5		

Completed by the Licensee

Figure space for the sampler

FIELD OPERATIONS MANUAL
BIOLOGICS PROGRAM
CHAPTER 9
PRODUCT DESTRUCTION

PRODUCT DESTRUCTION

CONTENTS

Page
AUTHORITY FOR PRODUCT DESTRUCTION.......... 2
DISPOSAL METHODS - PRODUCTS CONTAINING LIVE AGENTS OR TOXINS.......... 2
  Incineration.......... 2
  Dry Heat.......... 2
  Autoclaving.......... 2
  Chemical Inactivation.......... 2
DISPOSAL METHODS - REFUSE, CARCASSES, UNDESIRABLE BY-PRODUCTS CONTAINING LIVE AGENTS OR TOXINS.......... 2
  Rendering.......... 2
  Burial.......... 2
  Transport of Materials.......... 2
PRODUCTS FOUND UNSATISFACTORY BY VS TESTING.......... 2
  VS Form 14-45.......... 3
PRODUCTS FOUND UNSATISFACTORY BY LICENSEES.......... 3
  VS Form 14-8 Block 13.......... 3
OTHER TYPES OF PRODUCTS OR BY-PRODUCTS.......... 3
DISPOSAL ROUTINES.......... 3
VS MEMO 800.56.......... 4
TRAINING IN PRODUCT DESTRUCTION.......... 4

PRODUCT DESTRUCTION

AUTHORITY FOR PRODUCT DESTRUCTION

The Virus-Serum-Toxin Act makes it unlawful to prepare or sell worthless, dangerous, contaminated, or harmful products for use in domestic animals. 9 CFR 114.15 requires that all biological products that are found to be unsatisfactory for marketing, all refuse or other material deemed unsatisfactory for production purposes, all carcasses (part or whole) of production or test animals, and all undesirable by-products of manufacture be disposed of under rules established by the Deputy Administrator so that the intent of the Act can be fully realized.

DISPOSAL METHODS

The way product is handled depends upon: (1) whether the product contains live agents or toxins or is inactivated, and (2) whether it has been found unsatisfactory by VS testing or by licensee testing.

PRODUCTS CONTAINING LIVE AGENTS OR TOXINS

Because live agents or toxins may be potentially hazardous to the health of humans, or other animals, or the environment, they must be inactivated by approved procedures. Serials found contaminated are considered to contain live agents. The following methods are approved:

Incineration	This requires the application of flame to the product for enough time to insure all infectious or toxic agents are made non-infectious or non-toxic.
Dry Heat	This requires applying enough heat to the product to insure that all containers are heated to at least 160° C (320° F) for at least one hour.
Autoclaving	This requires using enough live steam so that the steam has a chance to penetrate all parts of the product for at least one half hour at a temperature of at least 120° C (248° F)
Chemical	This requires the addition of enough chemicals such as formalin, phenol, cresol, beta-propiolactone, phenylmercuric nitrate, etc. to the product and allowing sufficient time for the chemicals to act to insure that contamination in the product does not exceed what would be allowed in a satisfactory product.

REFUSE, CARCASSES, AND OTHER UNDESIRABLE BY-PRODUCTS WHICH MAY CONTAIN LIVE AGENTS OR TOXINS

The by-products of biologics manufacture (such as refuse, carcasses, contaminated disposable plasticware, etc.) may also contain live agents or toxins. Care and good practice must also govern the disposal of this type of material. The following methods of disposal are approved ways:

Rendering	This requires the denaturing and cooking of carcasses or other organic material in closed tanks for enough time to make the material unusable for human food. Infectious organisms are destroyed in the process.
Burial	This requires the careful placement of material in the ground below ground level and then covering with enough covering material to insure infectious agents or toxins are not further spread.
	Other methods approved for product disposal can also be used.
Transport of Materials	Be sure vehicles used to transport infectious material are constructed so as to be leak-proof and that they can be and are effectively cleaned and disinfected after use.

PRODUCTS FOUND UNSATISFACTORY BY VS TESTING

It is VS policy to have VS personnel physically present at the firm to personally observe the destruction of product that has been found unsatisfactory as a result of VS testing. Unsatisfactory serials are reported to the licensee by VS on the VS Form 14-8. The VS Form 14-14 reports the details of VS testing, eg. contamination, low potency. VS Form 14-45 PRODUCT DESTRUCTION RECORD form is completed by the VS observer to certify disposal. See Figure 9-1.

VS Form 14-45

Use VS 14-45 only for recording destruction of serials found unsatisfactory by VSL. Do not use (or provide blank forms for use by the licensee) to record destruction of serials found unsatisfactory by the licensee.

Note that block 4C of the form is the number of containers reported in the VS 14-8 inventory while block 4E shows the exact tally that was destroyed. These two tallies will usually vary.

Complete the form after destruction has been carried out. Send the yellow copy to Biologics Data Center, Box 844, Ames, IA 50010. Send the original to the AVIC for filing. Leave the pink copy with the licensee and retain the golden copy for yourself.

PRODUCTS FOUND UNSATISFACTORY BY LICENSEES

VS policy does not require licensees to destroy under VS supervision products that have been found unsatisfactory as a result of licensee testing.

VS Form 14-8
Block 13

Note that report of destruction of product by the firm is reported in block 13 of VS Form 14-8.

Note also that notice of destruction on the VS 14-8 is not an intent to destroy but a certification of destruction. "Destroyed" product should not be later found in a licensee's cooler!

OTHER TYPES OF PRODUCTS OR BY-PRODUCTS

Products or by-products not containing live agents or toxins are subject only to applicable federal, state, or local laws and regulations pertaining to the treatment and disposal of waste and to environmental quality.

Fill out a VS Form 14-45 for inactivated products after witnessing the destruction of such products found unsatisfactory as a result of VS testing.

If a sanitary landfill is used, check during an inspection to verify that the landfill is run properly and that unsatisfactory product is, in fact, destroyed.

DISPOSAL ROUTINES

The licensee will notify the sampler or other VS employee when a serial is to be destroyed under VS supervision. The responsibility of the VS observer is as follows:

Schedule product destruction as part of a normally scheduled sampling or other routine visit to the firm. Do not make a special trip.

Request to see the firm's copy of VS Forms 14-8 and VS Forms 14-14 for each serial or subserial to be destroyed.

Ask what method of destruction the firm proposes to use.

Determine if the method is allowed in VS Memo 800.56 before O.K.'ing.

Be sure the entire inventory is presented for destruction. This should include all reserve and retention samples. To retain any portion of an unsatisfactory serial, the licensee must obtain written permission from the AVIC prior to presenting the serial for destruction.

Make an actual count of the serial.

Keep the inventory under your observation and control until the destruction cycle has progressed enough to make all product unmarketable. This, for example, can mean until the heat of the autoclave or incinerator has been applied. You may wish to sample or do other duties while destruction cycle is under way.

Observe completion of cycle, i.e. removal from the autoclave or incinerator, actual burial, etc.

Certify destruction by completing VS Form 14-45. Note any retained samples on the VS 14-45.

VS MEMO 800.56

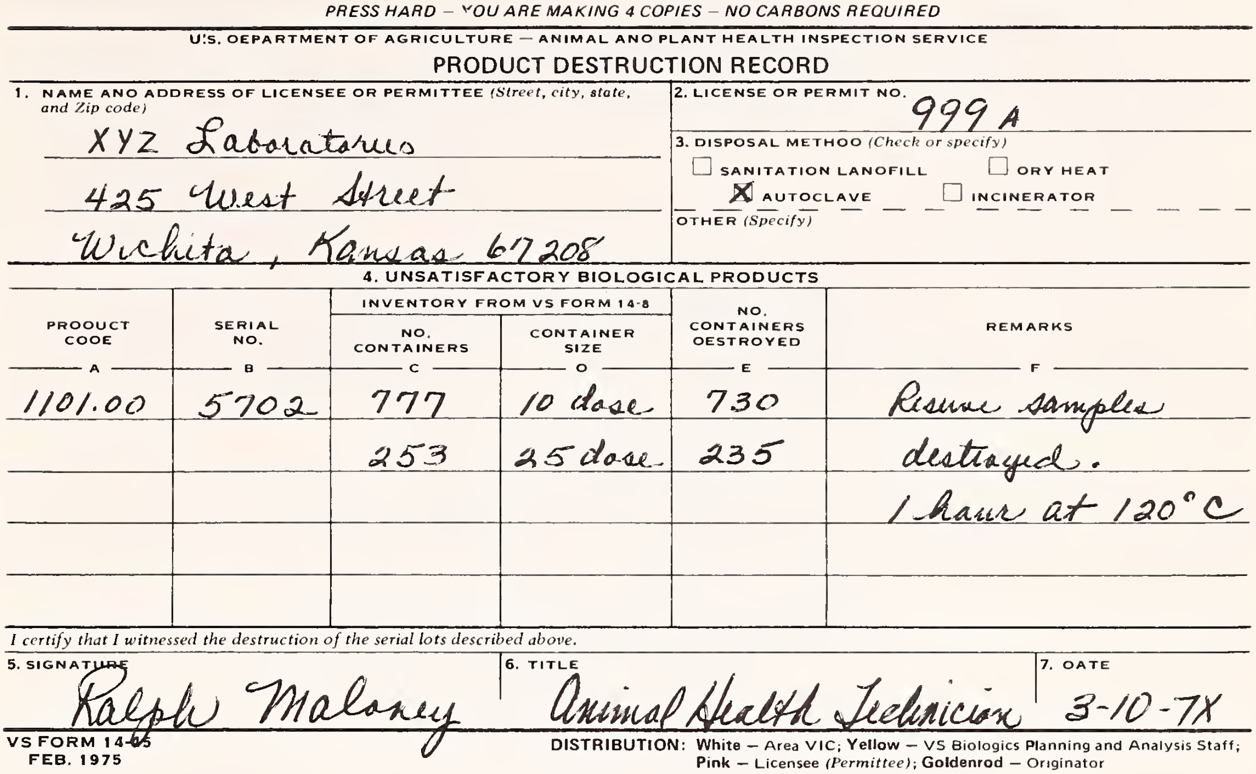
VS Memo 800.56 contains policy on Product Destruction. Note the Virus-Serum-Toxin Act prohibits preparation and sale of unsatisfactory product. The decision to destroy such products can be made only by an authorized agent of the licensee. Once decided upon, destruction must be by approved methods.

TRAINING IN PRODUCT DESTRUCTION

The Regional Biologics Specialist (RBS) has been assigned to each Area in which product destruction is being done. The RBS trains, advises, and instructs VS employees and contractors in the methods, procedures, and policies used in proper product destruction.

Contact your RBS through the AVIC if you have questions involving product destruction or if training or review in proper methods is required.

FIGURE 9-1



PRESS HARD — YOU ARE MAKING 4 COPIES — NO CARBONS REQUIRED

U.S. DEPARTMENT OF AGRICULTURE — ANIMAL AND PLANT HEALTH INSPECTION SERVICE

PRODUCT DESTRUCTION RECORD

1. NAME AND ADDRESS OF LICENSEE OR PERMITTEE *(Street, city, state, and Zip code)*

XYZ Laboratories
425 West Street
Wichita, Kansas 67208

2. LICENSE OR PERMIT NO. 999 A

3. DISPOSAL METHOD *(Check or specify)*

☐ SANITATION LANDFILL ☐ DRY HEAT
☒ AUTOCLAVE ☐ INCINERATOR
OTHER *(Specify)*

4. UNSATISFACTORY BIOLOGICAL PRODUCTS

PRODUCT CODE A	SERIAL NO. B	INVENTORY FROM VS FORM 14-8 NO. CONTAINERS C	INVENTORY FROM VS FORM 14-8 CONTAINER SIZE D	NO. CONTAINERS DESTROYED E	REMARKS F
1101.00	5702	777	10 dose	730	Reserve samples
		253	25 dose	235	destroyed.
					1 hour at 120°C

I certify that I witnessed the destruction of the serial lots described above.

5. SIGNATURE Ralph Maloney

6. TITLE Animal Health Technician

7. DATE 3-10-7X

VS FORM 14-05
FEB. 1975

DISTRIBUTION: White — Area VIC; Yellow — VS Biologics Planning and Analysis Staff; Pink — Licensee *(Permittee)*; Goldenrod — Originator

FIGURE 9-2

FORM APPROVED: OMB NO. 40-R2582

U.S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY BIOLOGICS PRODUCTION AND TEST REPORT

NOTE: Submit an original and three copies for every serial or subserial which reaches any stage of identification and testing.

1. HARVEST DATE 5-8-7X	2. PAGE 1 OF 1
3. LYOPHILIZATION DATE 6-19-7X	4. LICENSE OR PERMIT NO. 999A
6. EXPIRATION DATE 7-12-7X	7. PRODUCT CODE NO. 1101.00
8. PRODUCING SUBSIDIARY	9. SERIAL OR SUBSERIAL NO. 5702

5. NAME & MAILING ADDRESS OF LICENSEE OR PERMITTEE *(Include zip code)*

XYZ Laboratories
425 West Street
Wichita, Kansas 67208

10. TRUE NAME OF PRODUCT

Bovine Rhinotracheitis Vaccine

11. TEST DATA *(For additional test data, use VS Form 14-8 A)*

INSERT CODE: S - SATISFACTORY, U - UNSATISFACTORY, I - INCONCLUSIVE, NT - NO TEST

TEST REFERENCE A	TEST DATES STARTED B	TEST DATES CONCLUDED C	RESULTS D	E
113.27(a)(4)	6-19-7X	6-26-7X	10/10 No Growth	S
113.27(a)(5)	6-19-7X	7-2-7X	10/10 No Growth	S
113.33(a)	6-19-7X	6-26-7X	IC 8/8 well; IP 8/8 well	S
113.41 all	6-19-7X	7-9-7X	2/2 well	S
113.145(d)(3)	6-28-7X	7-2-7X	$10^{4.8}$ $TCID_{50}S$ per dose	S
113.135(c)(2)	6-28-7X	7-2-7X	IBR virus identified by SN test	S
113.28 all	6-19-7X	7-12-7X	No mycoplasma detected	S
113.29 all	6-26-7X	6-28-7X	0.92%	S

12. INVENTORY FOR RELEASE *(Use a separate line for each size container)*

NO. OF CONTAINERS A	CONTAINER SIZE (DOSES CC OR UNITS) B	TOTAL QUANTITY (CC OR UNITS) C	TOTAL NO. DOSES D	REMARKS E
777	10 dose	15,540	7,770	
253	25 dose	13,750	6,325	
TOTAL 1,030	▨	TOTAL 28,290	TOTAL 14,095	

13. DISPOSITION BY FIRM ☒ ELIGIBLE FOR RELEASE ☐ DESTROYED ☐ TO BE REPROCESSED AND RETESTED
☐ OTHER *(Explain)*

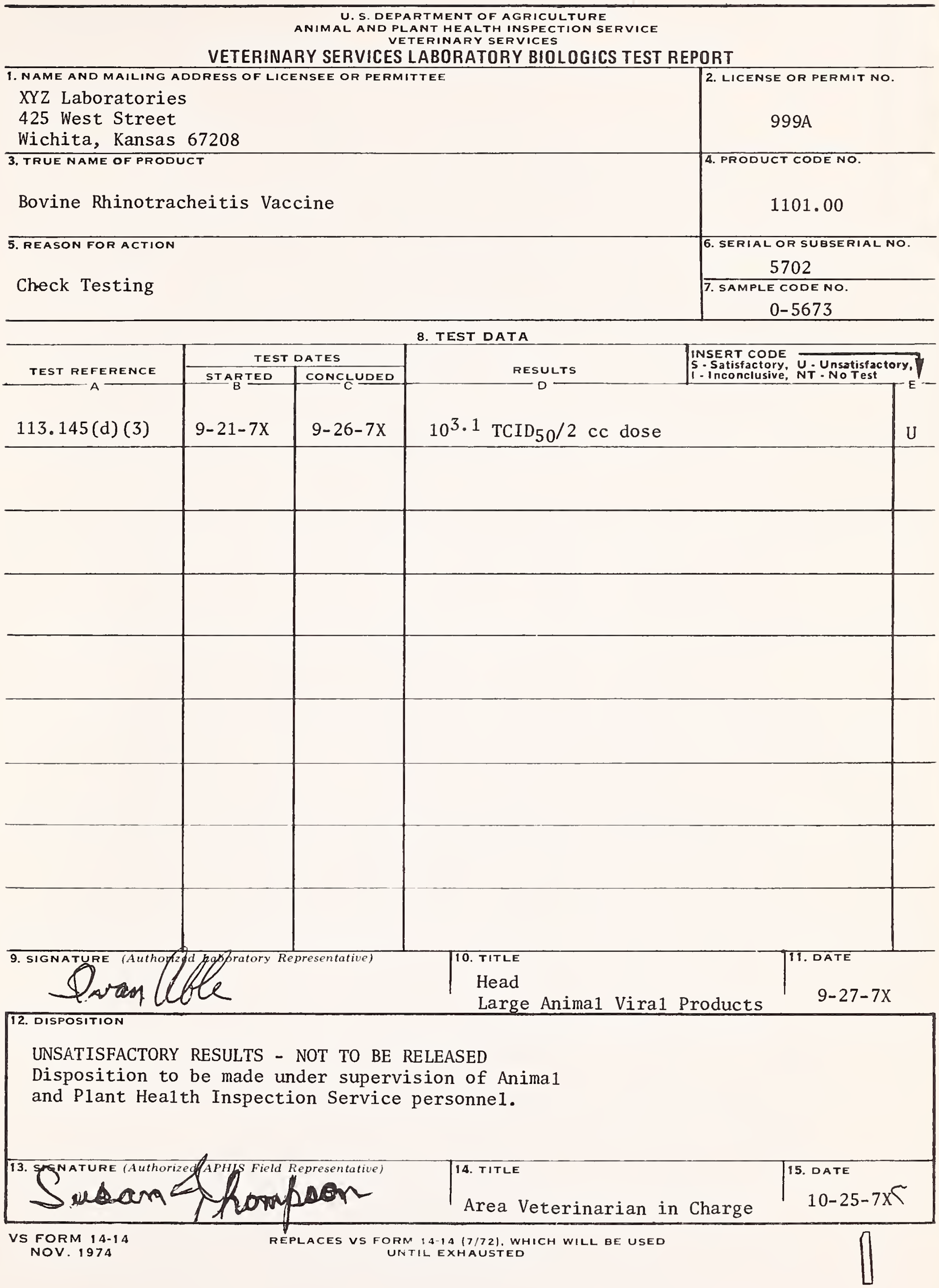
14. SIGNATURE *(Authorized Firm Representative)* P.F. Sharp	15. TITLE Director of Control	16. DATE 7-22-7X

17. DISPOSITION BY APHIS ☐ NOT TO BE TESTED ☐ TESTS COMPLETED, SATISFACTORY
☒ TESTS COMPLETED, UNSATISFACTORY *(Explain)* ☐ OTHER *(Explain)*
NOT TO BE RELEASED - Disposition to be made under supervision of Animal and Plant Health Inspection Service personnel.

18. SIGNATURE *(Authorized APHIS Representative)* Susan Thompson	19. TITLE Area Veterinarian in Charge	20. DATE 10-25-7X

VS FORM 14-8 (11/74) PREVIOUS EDITIONS OBSOLETE

FIGURE 9-3



U. S. DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE
VETERINARY SERVICES

VETERINARY SERVICES LABORATORY BIOLOGICS TEST REPORT

1. NAME AND MAILING ADDRESS OF LICENSEE OR PERMITTEE
XYZ Laboratories
425 West Street
Wichita, Kansas 67208

2. LICENSE OR PERMIT NO.
999A

3. TRUE NAME OF PRODUCT
Bovine Rhinotracheitis Vaccine

4. PRODUCT CODE NO.
1101.00

5. REASON FOR ACTION
Check Testing

6. SERIAL OR SUBSERIAL NO.
5702

7. SAMPLE CODE NO.
0-5673

8. TEST DATA

TEST REFERENCE	TEST DATES		RESULTS	INSERT CODE S - Satisfactory, U - Unsatisfactory, I - Inconclusive, NT - No Test
	STARTED	CONCLUDED		
A	B	C	D	E
113.145(d)(3)	9-21-7X	9-26-7X	$10^{3.1}$ $TCID_{50}$/2 cc dose	U

9. SIGNATURE *(Authorized Laboratory Representative)*
Ivan Able

10. TITLE
Head
Large Animal Viral Products

11. DATE
9-27-7X

12. DISPOSITION
UNSATISFACTORY RESULTS - NOT TO BE RELEASED
Disposition to be made under supervision of Animal and Plant Health Inspection Service personnel.

13. SIGNATURE *(Authorized APHIS Field Representative)*
Susan Thompson

14. TITLE
Area Veterinarian in Charge

15. DATE
10-25-7X

VS FORM 14-14
NOV. 1974

REPLACES VS FORM 14-14 (7/72), WHICH WILL BE USED UNTIL EXHAUSTED